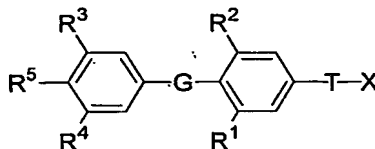


We Claim:

1. A compound of Formula I:



wherein:

- 5 G is selected from the group consisting of -O-, -S-, -S(=O)-, -S(=O)₂-, -CH₂-, -CF₂-, -CHF-, -C(O)-, -CH(OH)-, -NH-, and -N(C₁-C₄ alkyl)-;

- T is selected from the group consisting of -(CR^a₂)_k-, -CR^b=CR^b-(CR^a₂)_n-,
 -(CR^a₂)_n-CR^b=CR^b-, -(CR^a₂)_n-CR^b=CR^b-(CR^a₂)_n-, -O(CR^b₂)(CR^a₂)_n-,
 -S(CR^b₂)(CR^a₂)_n-, -N(R^c)(CR^b₂)(CR^a₂)_n-, -N(R^b)C(O)(CR^a₂)_n-,
 10 -(CR^a₂)_nCH(NR^bR^c)-, -C(O)(CR^a₂)_m-, -(CR^a₂)_mC(O)-, -(CR^a₂)C(O)(CR^a₂)_n-,
 -(CR^a₂)_nC(O)(CR^a₂)_p-, and -C(O)NH(CR^b₂)(CR^a₂)_p-;

k is an integer from 0-4;

m is an integer from 0-3;

n is an integer from 0-2;

- 15 p is an integer from 0-1;

- Each R^a is independently selected from the group consisting of hydrogen, optionally substituted -C₁-C₄ alkyl, halogen, -OH, optionally substituted -O-C₁-C₄ alkyl, -OCF₃, optionally substituted -S-C₁-C₄ alkyl, -NR^bR^c, optionally substituted -C₂-C₄ alkenyl, and optionally substituted -C₂-C₄ alkynyl; with the proviso
 20 that when one R^a is attached to C through an O, S, or N atom, then the other R^a attached to the same C is a hydrogen, or attached via a carbon atom;

Each R^b is independently selected from the group consisting of hydrogen and optionally substituted -C₁-C₄ alkyl;

- Each R^c is independently selected from the group consisting of hydrogen and
 25 optionally substituted -C₁-C₄ alkyl, optionally substituted -C(O)-C₁-C₄ alkyl, and -C(O)H;

- R¹ and R² are each independently selected from the group consisting of halogen, optionally substituted -C₁-C₄ alkyl, optionally substituted -S-C₁-C₃ alkyl, optionally substituted -C₂-C₄ alkenyl, optionally substituted -C₂-C₄ alkynyl, -CF₃, -OCF₃, optionally
 30 substituted -O-C₁-C₃ alkyl, and cyano;

R^3 and R^4 are each independently selected from the group consisting of hydrogen, halogen, $-CF_3$, $-OCF_3$, cyano, optionally substituted $-C_1-C_{12}$ alkyl, optionally substituted $-C_2-C_{12}$ alkenyl, optionally substituted $-C_2-C_{12}$ alkynyl, optionally substituted $-(CR^a_2)_m$ aryl, optionally substituted $-(CR^a_2)_m$ cycloalkyl, optionally substituted $-(CR^a_2)_m$ heterocycloalkyl, $-OR^d$, $-SR^d$, $-S(=O)R^e$, $-S(=O)_2R^e$, $-S(=O)_2NR^fR^g$, $-C(O)NR^fR^g$, $-C(O)OR^h$, $-C(O)R^e$, $-N(R^b)C(O)R^e$, $-N(R^b)C(O)NR^fR^g$, $-N(R^b)S(=O)_2R^e$, $-N(R^b)S(=O)_2NR^fR^g$, and $-NR^fR^g$;

Each R^d is selected from the group consisting of optionally substituted $-C_1-C_{12}$ alkyl, optionally substituted $-C_2-C_{12}$ alkenyl, optionally substituted $-C_2-C_{12}$ alkynyl, optionally substituted $-(CR^b_2)_n$ aryl, optionally substituted $-(CR^b_2)_n$ cycloalkyl, optionally substituted $-(CR^b_2)_n$ heterocycloalkyl, and $-C(O)NR^fR^g$;

Each R^e is selected from the group consisting of optionally substituted $-C_1-C_{12}$ alkyl, optionally substituted $-C_2-C_{12}$ alkenyl, optionally substituted $-C_2-C_{12}$ alkynyl, optionally substituted $-(CR^a_2)_n$ aryl, optionally substituted $-(CR^a_2)_n$ cycloalkyl, and optionally substituted $-(CR^a_2)_n$ heterocycloalkyl;

R^f and R^g are each independently selected from the group consisting of hydrogen, optionally substituted $-C_1-C_{12}$ alkyl, optionally substituted $-C_2-C_{12}$ alkenyl, optionally substituted $-C_2-C_{12}$ alkynyl, optionally substituted $-(CR^b_2)_n$ aryl, optionally substituted $-(CR^b_2)_n$ cycloalkyl, and optionally substituted $-(CR^b_2)_n$ heterocycloalkyl, or R^f and R^g may together form an optionally substituted heterocyclic ring, which may contain a second heterogroup selected from the group consisting of O, NR^c , and S, wherein said optionally substituted heterocyclic ring may be substituted with 0-4 substituents selected from the group consisting of optionally substituted $-C_1-C_4$ alkyl, $-OR^b$, oxo, cyano, $-CF_3$, optionally substituted phenyl, and $-C(O)OR^h$;

Each R^h is selected from the group consisting of optionally substituted $-C_1-C_{12}$ alkyl, optionally substituted $-C_2-C_{12}$ alkenyl, optionally substituted $-C_2-C_{12}$ alkynyl, optionally substituted $-(CR^b_2)_n$ aryl, optionally substituted $-(CR^b_2)_n$ cycloalkyl, and optionally substituted $-(CR^b_2)_n$ heterocycloalkyl;

R^5 is selected from the group consisting of $-OH$, optionally substituted $-OC_1-C_6$ alkyl, $-OC(O)R^e$, $-OC(O)OR^h$, $-F$, $-NHC(O)R^e$, $-NHS(=O)R^e$, $-NHS(=O)_2R^e$, $-NHC(=S)NH(R^h)$, and $-NHC(O)NH(R^h)$;

X is $P(O)YR^{11}Y'R^{11}$;

Y and Y' are each independently selected from the group consisting of $-O-$, and $-NR^v-$; when Y and Y' are $-O-$, R^{11} attached to $-O-$ is independently selected from

the group consisting of -H, alkyl, optionally substituted aryl, optionally substituted heterocycloalkyl, optionally substituted CH₂-heterocycloalkyl wherein the cyclic moiety contains a carbonate or thiocarbonate, optionally substituted -alkylaryl,

- C(R^z)₂OC(O)NR^z₂, -NR^z-C(O)-R^y, -C(R^z)₂-OC(O)R^y,
 5 -C(R^z)₂-O-C(O)OR^y, -C(R^z)₂OC(O)SR^y, -alkyl-S-C(O)R^y, -alkyl-S-S-alkylhydroxy,
 and -alkyl-S-S-S-alkylhydroxy;

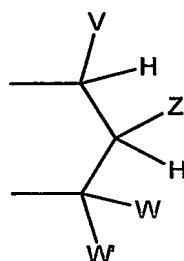
when Y and Y' are -NR^v-, then R¹¹ attached to -NR^v- is independently selected from the group consisting

- of -H, -[C(R^z)₂]_q-COOR^y, -C(R^x)₂COOR^y, -[C(R^z)₂]_q-C(O)SR^y,
 10 and -cycloalkylene-COOR^y;

when Y is -O- and Y' is NR^v-, then R¹¹ attached to -O- is independently selected from the group consisting of -H, alkyl, optionally substituted aryl, optionally substituted heterocycloalkyl, optionally substituted CH₂-heterocycloalkyl wherein the cyclic moiety contains a carbonate or thiocarbonate, optionally

- substituted -alkylaryl, -C(R^z)₂OC(O)NR^z₂, -NR^z-C(O)-R^y, -C(R^z)₂-OC(O)R^y,
 15 -C(R^z)₂-O-C(O)OR^y, -C(R^z)₂OC(O)SR^y, -alkyl-S-C(O)R^y, -alkyl-S-S-alkylhydroxy,
 and -alkyl-S-S-S-alkylhydroxy; and R¹¹ attached to -NR^v- is independently selected from the group consisting of -H, -[C(R^z)₂]_q-COOR^y, -C(R^x)₂COOR^y, -[C(R^z)₂]_q-C(O)SR^y,
 and -cycloalkylene-COOR^y;

- 20 or when Y and Y' are independently selected from -O- and -NR^v-, then together R¹¹ and R¹¹ are -alkyl-S-S-alkyl- to form a cyclic group, or together R¹¹ and R¹¹ are the group:



wherein:

- 25 V, W, and W' are independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted aralkyl, heterocycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, optionally substituted 1-alkenyl, and optionally substituted 1-alkynyl;

- or together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 atoms, wherein 0-1 atoms are heteroatoms and the remaining atoms are carbon, substituted with hydroxy, acyloxy, alkylthiocarbonyloxy, alkoxy carbonyloxy, or aryloxy carbonyloxy attached to a carbon atom that is three atoms from both Y groups attached to the phosphorus; or
- or together V and Z are connected via an additional 3-5 atoms to form a cyclic group, wherein 0-1 atoms are heteroatoms and the remaining atoms are carbon, that is fused to an aryl group at the beta and gamma position to the Y attached to the phosphorus;
- or together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxy carbonyloxy, alkylthiocarbonyloxy, and aryloxy carbonyloxy, attached to one of said carbon atoms that is three atoms from a Y attached to the phosphorus;
- or together Z and W are connected via an additional 3-5 atoms to form a cyclic group, wherein 0-1 atoms are heteroatoms and the remaining atoms are carbon, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;
- or together W and W' are connected via an additional 2-5 atoms to form a cyclic group, wherein 0-2 atoms are heteroatoms and the remaining atoms are carbon, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;
- Z is selected from the group consisting of $-\text{CHR}^z\text{OH}$, $-\text{CHR}^z\text{OC}(\text{O})\text{R}^y$, $-\text{CHR}^z\text{OC}(\text{S})\text{R}^y$, $-\text{CHR}^z\text{OC}(\text{S})\text{OR}^y$, $-\text{CHR}^z\text{OC}(\text{O})\text{SR}^y$, $-\text{CHR}^z\text{OCO}_2\text{R}^y$, $-\text{OR}^z$, $-\text{SR}^z$, $-\text{CHR}^z\text{N}_3$, $-\text{CH}_2\text{aryl}$, $-\text{CH}(\text{aryl})\text{OH}$, $-\text{CH}(\text{CH}=\text{CR}^z_2)\text{OH}$, $-\text{CH}(\text{C}=\text{CR}^z_2)\text{OH}$, $-\text{R}^z$, $-\text{NR}^z_2$, $-\text{OCOR}^y$, $-\text{OCO}_2\text{R}^y$, $-\text{SCOR}^y$, $-\text{SCO}_2\text{R}^y$, $-\text{NHCOR}^z$, $-\text{NHCO}_2\text{R}^y$, $-\text{CH}_2\text{NHaryl}$, $-(\text{CH}_2)_q-\text{OR}^z$, and $-(\text{CH}_2)_q-\text{SR}^z$;
- q is an integer 2 or 3;
- Each R^z is selected from the group consisting of R^y and $-\text{H}$;
- Each R^y is selected from the group consisting of alkyl, aryl, heterocycloalkyl, and aralkyl;
- Each R^x is independently selected from the group consisting of $-\text{H}$, and alkyl, or together R^x and R^x form a cyclic alkyl group;
- Each R^v is selected from the group consisting of $-\text{H}$, lower alkyl, acyloxyalkyl, alkoxy carbonyloxyalkyl, and lower acyl;
- with the provisos that:

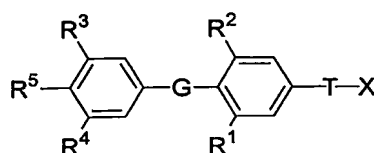
a) when G is -O-, T is -CH₂-, R¹ and R² are each bromo, R³ is *iso*-propyl, R⁴ is hydrogen, and R⁵ is -OH, then X is not P(O)(OH)₂ or P(O)(OCH₂CH₃)₂;

b) V, Z, W, W' are not all -H; and

c) when Z is -R^z, then at least one of V, W, and W' is not -H, alkyl, aralkyl, or heterocycloalkyl;

and pharmaceutically acceptable salts and prodrugs thereof and pharmaceutically acceptable salts of said prodrugs.

2. A compound of Formula I:



10 wherein:

G is selected from the group consisting of -O-, -S-, -S(=O)-, -S(=O)₂-, -CH₂-, -CF₂-, -CHF-, -C(O)-, -CH(OH)-, -NH-, and -N(C₁-C₄ alkyl)-;

T is selected from the group consisting of -(CR^a)_k-, -CR^b=CR^b-(CR^a)_n-, -(CR^a)_n-CR^b=CR^b-, -(CR^a)₂-CR^b=CR^b-(CR^a)₂-, -O(CR^b)₂(CR^a)_n-,
 15 -S(CR^b)₂(CR^a)_n-, -N(R^c)(CR^b)₂(CR^a)_n-, -N(R^b)C(O)(CR^a)_n-,
 -(CR^a)_nCH(NR^bR^c)-, -C(O)(CR^a)_m-, -(CR^a)_mC(O)-, -(CR^a)₂C(O)(CR^a)_n-,
 -(CR^a)_nC(O)(CR^a)₂-, and -C(O)NH(CR^b)₂(CR^a)_p-;

k is an integer from 0-4;

m is an integer from 0-3;

20 n is an integer from 0-2;

p is an integer from 0-1;

Each R^a is independently selected from the group consisting of hydrogen, optionally substituted -C₁-C₄ alkyl, halogen, -OH, optionally substituted -O-C₁-C₄ alkyl, -OCF₃, optionally substituted -S-C₁-C₄ alkyl, -NR^bR^c, optionally
 25 substituted -C₂-C₄ alkenyl, and optionally substituted -C₂-C₄ alkynyl; with the proviso that when one R^a is attached to C through an O, S, or N atom, then the other R^a attached to the same C is a hydrogen, or attached via a carbon atom;

Each R^b is independently selected from the group consisting of hydrogen and optionally substituted -C₁-C₄ alkyl;

Each R^c is independently selected from the group consisting of hydrogen, optionally substituted $-C_1-C_4$ alkyl, optionally substituted $-C(O)-C_1-C_4$ alkyl, and $-C(O)H$;

R^1 and R^2 are each independently selected from the group consisting of halogen, optionally substituted $-C_1-C_4$ alkyl, optionally substituted $-S-C_1-C_3$ alkyl, optionally substituted $-C_2-C_4$ alkenyl, optionally substituted $-C_2-C_4$ alkynyl, $-CF_3$, $-OCF_3$, optionally substituted $-O-C_1-C_3$ alkyl, and cyano;

R^3 and R^4 are each independently selected from the group consisting of hydrogen, halogen, $-CF_3$, $-OCF_3$, cyano, optionally substituted $-C_1-C_{12}$ alkyl, optionally substituted $-C_2-C_{12}$ alkenyl, optionally substituted $-C_2-C_{12}$ alkynyl, optionally substituted $-(CR^a)_m$ aryl, optionally substituted $-(CR^a)_m$ cycloalkyl, optionally substituted $-(CR^a)_m$ heterocycloalkyl, $-OR^d$, $-SR^d$, $-S(=O)R^e$, $-S(=O)_2R^e$, $-S(=O)_2NR^fR^g$, $-C(O)NR^fR^g$, $-C(O)OR^h$, $-C(O)R^e$, $-N(R^b)C(O)R^e$, $-N(R^b)C(O)NR^fR^g$, $-N(R^b)S(=O)_2R^e$, $-N(R^b)S(=O)_2NR^fR^g$, and $-NR^fR^g$;

Each R^d is selected from the group consisting of optionally substituted $-C_1-C_{12}$ alkyl, optionally substituted $-C_2-C_{12}$ alkenyl, optionally substituted $-C_2-C_{12}$ alkynyl, optionally substituted $-(CR^b)_n$ aryl, optionally substituted $-(CR^b)_n$ cycloalkyl, optionally substituted $-(CR^b)_n$ heterocycloalkyl, and $-C(O)NR^fR^g$;

Each R^e is optionally substituted $-C_1-C_{12}$ alkyl, optionally substituted $-C_2-C_{12}$ alkenyl, optionally substituted $-C_2-C_{12}$ alkynyl, optionally substituted $-(CR^a)_n$ aryl, optionally substituted $-(CR^a)_n$ cycloalkyl, and optionally substituted $-(CR^a)_n$ heterocycloalkyl;

R^f and R^g are each independently selected from the group consisting of hydrogen, optionally substituted $-C_1-C_{12}$ alkyl, optionally substituted $-C_2-C_{12}$ alkenyl, optionally substituted $-C_2-C_{12}$ alkynyl, optionally substituted $-(CR^b)_n$ aryl, optionally substituted $-(CR^b)_n$ cycloalkyl, and optionally substituted $-(CR^b)_n$ heterocycloalkyl, or R^f and R^g may together form an optionally substituted heterocyclic ring, which may contain a second heterogroup selected from the group of O, NR^c , and S, wherein said optionally substituted heterocyclic ring may be substituted with 0-4 substituents selected from the group consisting of optionally substituted $-C_1-C_4$ alkyl, $-OR^b$, oxo, cyano, $-CF_3$, optionally substituted phenyl, and $-C(O)OR^h$;

Each R^h is selected from the group consisting of optionally substituted $-C_1-C_{12}$ alkyl, optionally substituted $-C_2-C_{12}$ alkenyl, optionally substituted $-C_2-C_{12}$ alkynyl,

optionally substituted $-(CR^b)_n$ aryl, optionally substituted $-(CR^b)_n$ cycloalkyl, and optionally substituted $-(CR^b)_n$ heterocycloalkyl;

R^5 is selected from the group consisting of -OH, optionally substituted $-OC_1-C_6$ alkyl, $-OC(O)R^e$, $-OC(O)OR^h$, -F, $-NHC(O)R^e$, $-NHS(=O)R^e$, $-NHS(=O)_2R^e$,
 5 $-NHC(=S)NH(R^h)$, and $-NHC(O)NH(R^h)$;

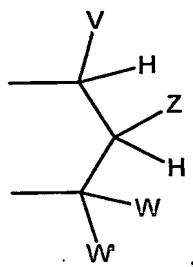
X is $P(O)YR^{11}Y'R^{11}$;

Y and Y' are each independently selected from the group consisting of -O-, and $-NR^v$ -; when Y and Y' are -O-, R^{11} attached to -O- is independently selected from the group consisting of -H, alkyl, optionally substituted aryl, optionally substituted
 10 heterocycloalkyl, optionally substituted CH_2 -heterocycloalkyl wherein the cyclic moiety contains a carbonate or thiocarbonate, optionally substituted -alkylaryl, $-C(R^z)_2OC(O)NR^z$, $-NR^z-C(O)-R^y$, $-C(R^z)_2-OC(O)R^y$, $-C(R^z)_2-O-C(O)OR^y$, $-C(R^z)_2OC(O)SR^y$, -alkyl-S-C(O) R^y , -alkyl-S-S-alkylhydroxy, and -alkyl-S-S-S-alkylhydroxy;

15 when Y and Y' are $-NR^v$ -, then R^{11} attached to $-NR^v$ - is independently selected from the group consisting of -H, $-[C(R^z)_2]_q-COOR^y$, $-C(R^x)_2COOR^y$, $-[C(R^z)_2]_q-C(O)SR^y$, and -cycloalkylene-COOR y ;

when Y is -O- and Y' is $-NR^v$ -, then R^{11} attached to -O- is independently selected
 20 from the group consisting of -H, alkyl, optionally substituted aryl, optionally substituted heterocycloalkyl, optionally substituted CH_2 -heterocycloalkyl wherein the cyclic moiety contains a carbonate or thiocarbonate, optionally substituted -alkylaryl, $-C(R^z)_2OC(O)NR^z$, $-NR^z-C(O)-R^y$, $-C(R^z)_2-OC(O)R^y$, $-C(R^z)_2-O-C(O)OR^y$, $-C(R^z)_2OC(O)SR^y$, -alkyl-S-C(O) R^y , -alkyl-S-S-alkylhydroxy, and -alkyl-S-S-S-alkylhydroxy; and R^{11} attached to $-NR^v$ - is independently selected from
 25 the group consisting of -H, $-[C(R^z)_2]_q-COOR^y$, $-C(R^x)_2COOR^y$, $-[C(R^z)_2]_q-C(O)SR^y$, and -cycloalkylene-COOR y ;

or when Y and Y' are independently selected from -O- and $-NR^v$ -, then together R^{11} and R^{11} are -alkyl-S-S-alkyl- to form a cyclic group, or together R^{11} and R^{11} are the
 30 group: ;



wherein:

V, W, and W' are independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted aralkyl, heterocycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, optionally substituted 1-alkenyl, and optionally substituted 1-alkynyl;

or together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 atoms, wherein 0 – 1 atoms are heteroatoms and the remaining atoms are carbon, substituted with hydroxy, acyloxy, alkylthiocarbonyloxy, alkoxy carbonyloxy, or aryloxy carbonyloxy attached to a carbon atom that is three atoms from both Y groups attached to the phosphorus; or

or together V and Z are connected via an additional 3-5 atoms to form a cyclic group, wherein 0–1 atoms are heteroatoms and the remaining atoms are carbon, that is fused to an aryl group at the beta and gamma position to the Y attached to the phosphorus;

or together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxy carbonyloxy, alkylthiocarbonyloxy, and aryloxy carbonyloxy, attached to one of said carbon atoms that is three atoms from a Y attached to the phosphorus;

or together Z and W are connected via an additional 3-5 atoms to form a cyclic group, wherein 0–1 atoms are heteroatoms and the remaining atoms are carbon, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

or together W and W' are connected via an additional 2-5 atoms to form a cyclic group, wherein 0–2 atoms are heteroatoms and the remaining atoms are carbon, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

Z is selected from the group consisting of $-\text{CHR}^z\text{OH}$, $-\text{CHR}^z\text{OC(O)}\text{R}^y$, $-\text{CHR}^z\text{OC(S)}\text{R}^y$, $-\text{CHR}^z\text{OC(S)}\text{OR}^y$, $-\text{CHR}^z\text{OC(O)}\text{SR}^y$, $-\text{CHR}^z\text{OCO}_2\text{R}^y$, $-\text{OR}^z$,

- SR^z, -CHR^zN₃, -CH₂aryl, -CH(aryl)OH, -CH(CH=CR^z)OH, -CH(C≡CR^z)OH, -R^z, -NR^z, -OCOR^y, -OCO₂R^y, -SCOR^y, -SCO₂R^y, -NHCOR^z, -NHCO₂R^y, -CH₂NHaryl, -(CH₂)_q-OR^z, and -(CH₂)_q-SR^z;
- q is an integer 2 or 3;
- 5 Each R^z is selected from the group consisting of R^y and -H;
- Each R^y is selected from the group consisting of alkyl, aryl, heterocycloalkyl, and aralkyl;
- Each R^x is independently selected from the group consisting of -H, and alkyl, or together R^x and R^x form a cyclic alkyl group;
- 10 Each R^y is selected from the group consisting of -H, lower alkyl, acyloxyalkyl, alkoxy carbonyloxyalkyl, and lower acyl;
- with the provisos that:
- a) when G is -O-, T is -(CH₂)₀₋₄-, R¹ and R² are independently halogen, alkyl of 1 to 3 carbons, and cycloalkyl of 3 to 5 carbons, R³ is alkyl of 1 to 4 carbons or cycloalkyl of 3 to 7 carbons, R⁴ is hydrogen, and R⁵ is -OH, then X is not -P(O)(OH)₂ or -P(O)(O-lower alkyl)₂;
- 15 b) when G is -O-, R⁵ is -NHC(O)R^e, -NHS(=O)₁₋₂R^e, -NHC(S)NH(R^h), or -NHC(O)NH(R^h), T is -(CH₂)_m-, -CH=CH-, -O(CH₂)₁₋₂-, or -NH(CH₂)₁₋₂-, then X is not -P(O)(OH)₂ or -P(O)(OH)NH₂;
- 20 c) V, Z, W, W' are not all -H; and
- d) when Z is -R^z, then at least one of V, W, and W' is not -H, alkyl, aralkyl, or heterocycloalkyl;
- and pharmaceutically acceptable salts and prodrugs thereof and pharmaceutically acceptable salts of said prodrugs.
- 25 3. The compound of claim 1 wherein when G is -O-, T is -CH₂-, R¹ and R² are each bromo, R³ is *iso*-propyl, and R⁵ is -OH, then R⁴ is not hydrogen.
4. The compound of claim 2 wherein when G is -O-, T is -(CH₂)₀₋₄-, R¹ and R² are independently selected from the group consisting of halogen, alkyl of 1 to 3 carbons, and cycloalkyl of 3 to 5 carbons, R³ is alkyl of 1 to 4 carbons or cycloalkyl of 3 to 7 carbons, and R⁵ is -OH, then R⁴ is not hydrogen; and wherein when G is -O-, R⁵ is selected from the group consisting of NHC(O)R^e, -NHS(=O)₁₋₂R^e, -NHC(=S)NH(R^h), and -NHC(O)NH(R^h), T is selected from the group consisting of -(CH₂)_m-, -CH=CH-, -O(CH₂)₁₋₂-, and -NH(CH₂)₁₋₂-, then R⁴ is not hydrogen.
- 30

5. The compound of claim 1 wherein G is selected from the group consisting of -O- and -CH₂-.
6. The compound of claim 2 wherein G is selected from the group consisting of -O- and -CH₂-.
- 5 7. The compound of claim 1 wherein T is selected from the group consisting of -(CR^a₂)_n-, -O(CR^b₂)(CR^a₂)_p-, -N(R^c)(CR^b₂)(CR^a₂)_p-, -S(CR^b₂)(CR^a₂)_p-, -NR^b(CO)-, and -CH₂CH(NR^cR^b)-.
8. The compound of claim 2 wherein T is selected from the group consisting of -(CR^a₂)_n-, -O(CR^b₂)(CR^a₂)_p-, -N(R^c)(CR^b₂)(CR^a₂)_p-, -S(CR^b₂)(CR^a₂)_p-, -NR^b(CO)-, 10 and -CH₂CH(NR^cR^b)-.
9. The compound of claim 1 wherein R¹ and R² are the same and are selected from the group consisting of halogen, -C₁-C₄ alkyl, -CF₃, and cyano.
10. The compound of claim 2 wherein R¹ and R² are the same and are selected from the group consisting of halogen, -C₁-C₄ alkyl, -CF₃, and cyano.
- 15 11. The compound of claim 1 wherein R¹ and R² are different and are selected from the group consisting of halogen, -C₁-C₄ alkyl, -CF₃, and cyano.
12. The compound of claim 2 wherein R¹ and R² are different and are selected from the group consisting of halogen, -C₁-C₄ alkyl, -CF₃, and cyano.
13. The compound of claim 1 wherein R⁴ is selected from the group 20 consisting of hydrogen, halogen, -C₁-C₄ alkyl, cyano and CF₃.
14. The compound of claim 2 wherein R⁴ is selected from the group consisting of hydrogen, halogen, -C₁-C₄ alkyl, cyano, and CF₃.
15. The compound of claim 1 wherein R⁵ is selected from the group consisting of -OH, -OC(O)R^e, -OC(O)OR^h, -F, and -NHC(O)R^e.
- 25 16. The compound of claim 2 wherein R⁵ is selected from the group consisting of -OH, -OC(O)R^e, -OC(O)OR^h, -F, and -NHC(O)R^e.
17. The compound of claim 1 wherein R³ is selected from the group consisting of halogen, optionally substituted -C₁-C₆ alkyl, -CF₃, cyano, -C(O)NR^fR^g, optionally substituted -(CR^a₂)_naryl, -SO₂NR^fR^g, and -SO₂R^e.
- 30 18. The compound of claim 2 wherein R³ is selected from the group consisting of halogen, optionally substituted -C₁-C₆ alkyl, -CF₃, cyano, -C(O)NR^fR^g, optionally substituted -(CR^a₂)_naryl, -SO₂NR^fR^g, and -SO₂R^e.
19. The compound of claim 1 wherein X is selected from the group consisting of -PO₃H₂, -P(O)[-OCR^z₂OC(O)R^y]₂, -P(O)[-OCR^z₂OC(O)OR^y]₂,

-P(O)[-N(H)CR^z₂C(O)OR^y]₂, -P(O)[-N(H)CR^z₂C(O)OR^y][-OR¹¹],
and -P(O)[-OCH(V)CH₂CH₂O-], wherein V is selected from the group consisting of optionally substituted aryl, aryl, heteroaryl, and optionally substituted heteroaryl.

20. The compound of claim 2 wherein X is selected from the group consisting of -PO₃H₂, -P(O)[-OCR^z₂OC(O)R^y]₂, -P(O)[-OCR^z₂OC(O)OR^y]₂,
-P(O)[-N(H)CR^z₂C(O)OR^y]₂, -P(O)[-N(H)CR^z₂C(O)OR^y][-OR¹¹],
and -P(O)[-OCH(V)CH₂CH₂O-], wherein V is selected from the group consisting of optionally substituted aryl, aryl, heteroaryl, and optionally substituted heteroaryl.

21. The compound of claim 1 wherein G is selected from the group consisting of -O- and -CH₂-; T is selected from the group consisting of -(CR^a₂)_n-, -O(CR^b₂)(CR^a₂)_p-, -N(R^c)(CR^b₂)(CR^a₂)_p-, -S(CR^b₂)(CR^a₂)_p-, -NR^b(CO)-, and -CH₂CH(NR^cR^b)-; R¹ and R² are each independently selected from the group consisting of halogen, -C₁-C₄ alkyl, -CF₃, and cyano; R⁴ is selected from the group consisting of hydrogen, halogen, -C₁-C₄ alkyl, cyano and CF₃; R⁵ is selected from the group consisting of -OH, -OC(O)R^e, -OC(O)OR^h, -F and -NHC(O)R^e; R³ is selected from the group consisting of halogen, optionally substituted -C₁-C₆ alkyl, -CF₃, cyano, -C(O)NR^fR^g, optionally substituted -(CR^a₂)_naryl, -SO₂NR^fR^g, and -SO₂R^e; and X is selected from the group consisting of -PO₃H₂, -P(O)[-OCR^z₂OC(O)R^y]₂,
-P(O)[-OCR^z₂OC(O)OR^y]₂, -P(O)[-N(H)CR^z₂C(O)OR^y]₂,
-P(O)[-N(H)CR^z₂C(O)OR^y][-OR¹¹] and -P(O)[-OCH(V)CH₂CH₂O-], wherein V is selected from the group consisting of optionally substituted aryl, aryl, heteroaryl, and optionally substituted heteroaryl.

22. The compound of claim 21 wherein when G is -O-, T is -CH₂-, R¹ and R² are bromo, R³ is *iso*-propyl, and R⁵ is -OH, then R⁴ is not hydrogen.

23. The compound of claim 2 wherein G is selected from the group consisting of -O- and -CH₂-; T is selected from the group consisting of -(CR^a₂)_n-, -O(CR^b₂)(CR^a₂)_p-, -N(R^c)(CR^b₂)(CR^a₂)_p-, -S(CR^b₂)(CR^a₂)_p-, -NR^b(CO)-, and -CH₂CH(NR^cR^b)-; R¹ and R² are each independently selected from the group consisting of halogen, -C₁-C₄ alkyl, -CF₃, and cyano; R⁴ is selected from the group consisting of hydrogen, halogen, -C₁-C₄ alkyl, cyano, and CF₃; R⁵ is selected from the group consisting of -OH, -OC(O)R^e, -OC(O)OR^h, -F and -NHC(O)R^e; R³ is selected from the group consisting of halogen, optionally substituted -C₁-C₆ alkyl, -CF₃, cyano, -C(O)NR^fR^g, optionally substituted (CR^a₂)_naryl, -SO₂NR^fR^g, and -SO₂R^e; and X is selected from the group consisting of -PO₃H₂, -P(O)[-OCR^z₂OC(O)R^y]₂, -P(O)[-OCR^z₂OC(O)OR^y]₂,

-P(O)[-N(H)CR^z₂C(O)OR^y]₂, -P(O)[-N(H)CR^z₂C(O)OR^y][-OR¹¹],
and -P(O)[-OCH(V)CH₂CH₂O-], wherein V is selected from the group consisting of
optionally substituted aryl, aryl, heteroaryl, and optionally substituted heteroaryl.

24. The compound of claim 23 wherein when G is -O-, T is -(CH₂)₀₋₂-, R¹ and
5 R² are independently selected from the group consisting of hydrogen, halogen, alkyl of 1
to 3 carbons, and cycloalkyl of 3 to 5 carbons, R³ is alkyl of 1 to 4 carbons or cycloalkyl
of 3 to 7 carbons, and R⁵ is -OH, then R⁴ is not hydrogen; and wherein when G is -O-,
R⁵ is

-NHC(O)R^e, T is selected from the group consisting of -(CH₂)_m-, -O(CH₂)₁₋₂-,
10 -NH(CH₂)₁₋₂-, then R⁴ is not hydrogen.

25. The compound of claim 21 wherein T is -CH₂CH(NH₂)-; R¹ and R² are
each independently selected from the group consisting of iodo, bromo, chloro, methyl,
and cyano; R⁴ is selected from the group consisting of hydrogen and halogen; R⁵ is
selected from the group consisting of -OH and -OC(O)R^e; and R³ is selected from the
15 group consisting of halogen, optionally substituted -C₁-C₆ alkyl, optionally
substituted -CH₂aryl, optionally substituted -CH(OH)aryl, -C(O)-amido, -S(=O)₂-amido,
wherein the amido group is selected from the group consisting of phenethylamino,
piperidiny, 4-methylpiperiziny, morpholinyl, cyclohexylamino, aniliny, and indolinyl,
and -SO₂R^e wherein R^e is selected from the group consisting of phenyl, 4-chlorophenyl,
20 4-fluorophenyl, and 4-pyridyl.

26. The compound of claim 25 wherein G is -O-; T is -CH₂CH(NH₂)-; R¹ and
R² are each iodo; R⁴ is selected from the group consisting of hydrogen and iodo; R⁵
is -OH; and R³ is iodo.

27. The compound of claim 26 wherein X is selected from the group
25 consisting of -PO₃H₂, -P(O)[-OCH₂OC(O)-*t*-butyl]₂, -P(O)[-OCH₂OC(O)O-*i*-propyl]₂,
-P(O)[-N(H)CH(CH₃)C(O)OCH₂CH₃]₂, -P(O)[-N(H)C(CH₃)₂C(O)OCH₂CH₃]₂,
-P(O)[-N(H)CH(CH₃)C(O)OCH₂CH₃][3,4-methylenedioxyphenyl],
-P(O)[-N(H)C(CH₃)₂C(O)OCH₂CH₃][3,4-methylenedioxyphenyl],
and -P(O)[-OCH(3-chlorophenyl)CH₂CH₂O-].

28. The compound of claim 21 wherein T is -N(H)C(O)-; R¹ and R² are each
30 independently selected from the group consisting of iodo, bromo, chloro, methyl, and
cyano; R⁴ is selected from the group consisting of hydrogen and iodo; R⁵ is selected from
the group consisting of -OH, and -OC(O)R^e; and R³ is selected from the group consisting
of iodo, bromo, optionally substituted -C₁-C₆ alkyl, optionally substituted -CH₂aryl,

optionally substituted -CH(OH)aryl, -C(O)-amido, -S(=O)₂-amido, wherein the amido group is selected from the group consisting of phenethylamino, piperidinyl, 4-methylpiperizinyl, morpholinyl, cyclohexylamino, anilinyl, and indolinyl, and -SO₂R^e wherein R^e is selected from the group consisting of phenyl, 4-chlorophenyl,

5 4-fluorophenyl, and 4-pyridyl.

29. The compound of claim 28 wherein G is -O-; R¹ and R² are each methyl; R⁴ is hydrogen; R⁵ is -OH; and R³ is -CH(OH)(4-fluorophenyl).

30. The compound of claim 29 wherein X is selected from the group consisting of -PO₃H₂, -P(O)[-OCH₂OC(O)-*t*-butyl]₂, -P(O)[-OCH₂OC(O)O-*i*-propyl]₂,
 10 -P(O)[-N(H)CH(CH₃)C(O)OCH₂CH₃]₂, -P(O)[-N(H)C(CH₃)₂C(O)OCH₂CH₃]₂,
 -P(O)[-N(H)CH(CH₃)C(O)OCH₂CH₃][3,4-methylenedioxyphenyl],
 -P(O)[-N(H)C(CH₃)₂C(O)OCH₂CH₃][3,4-methylenedioxyphenyl],
 and -P(O)[-OCH(3-chlorophenyl)CH₂CH₂O-].

31. The compound of claim 21 wherein T is -OCH₂-; R¹ and R² are each
 15 independently selected from the group consisting of iodo, bromo, chloro, methyl, and cyano; R⁴ is selected from the group consisting of hydrogen and iodo; R⁵ is selected from the group consisting of -OH, and -OC(O)R^e; and R³ is selected from the group consisting of iodo, bromo, optionally substituted C₁-C₆ alkyl, optionally substituted -CH₂aryl, optionally substituted -CH(OH)aryl, -C(O)-amido, -S(=O)₂-amido, wherein the amido
 20 group is selected from the group consisting of phenethylamino, piperidinyl, 4-methylpiperizinyl, morpholinyl, cyclohexylamino, anilinyl, and indolinyl, and -SO₂R^e wherein R^e is selected from the group consisting of phenyl, 4-chlorophenyl, 4-fluorophenyl, and 4-pyridyl.

32. The compound of claim 31 wherein G is -CH₂-; R¹ and R² are each
 25 methyl; R⁴ is hydrogen; R⁵ is -OH; and R³ is *iso*-propyl.

33. The compound of claim 32 wherein X is selected from the group consisting of -PO₃H₂, -P(O)[-OCH₂OC(O)-*t*-butyl]₂, -P(O)[-OCH₂OC(O)O-*i*-propyl]₂,
 -P(O)[-N(H)CH(CH₃)C(O)OCH₂CH₃]₂, -P(O)[-N(H)C(CH₃)₂C(O)OCH₂CH₃]₂,
 -P(O)[-N(H)CH(CH₃)C(O)OCH₂CH₃][3,4-methylenedioxyphenyl],
 30 -P(O)[-N(H)C(CH₃)₂C(O)OCH₂CH₃][3,4-methylenedioxyphenyl],
 and -P(O)[-OCH(3-chlorophenyl)CH₂CH₂O-].

34. The compound of claim 21 wherein T is -CH₂-; R¹ and R² are each independently selected from the group consisting of iodo, bromo, chloro, methyl, and cyano; R⁴ is selected from the group consisting of hydrogen and iodo; R⁵ is selected from

the group consisting of -OH, and -OC(O)R^e; and R³ is selected from the group consisting of iodo, bromo, optionally substituted C₁-C₆ alkyl, optionally substituted -CH₂aryl, optionally substituted -CH(OH)aryl, -C(O)-amido, -S(=O)₂-amido wherein the amido group is selected from the group consisting of phenethylamino, piperidinyl, 4-methylpiperizinyl, morpholinyl, cyclohexylamino, aniliny, and indolinyl, and -SO₂R^e wherein R^e is selected from the group consisting of phenyl, 4-chlorophenyl, 4-fluorophenyl, and 4-pyridyl.

35. The compound of claim 34 wherein when G is -O-, R¹ and R² are each bromo, R³ is *iso*-propyl, and R⁵ is -OH, then R⁴ is not hydrogen.

36. The compound of claim 34 wherein G is -O-; R¹ and R² are each chloro; R⁴ is hydrogen; R⁵ is -OH; and R³ is *i*-propyl.

37. The compound of claim 36 wherein X is selected from the group consisting of -PO₃H₂, -P(O)[-OCH₂OC(O)-*t*-butyl]₂, -P(O)[-OCH₂OC(O)O-*i*-propyl]₂, -P(O)[-N(H)CH(CH₃)C(O)OCH₂CH₃]₂, -P(O)[-N(H)C(CH₃)₂C(O)OCH₂CH₃]₂, -P(O)[-N(H)CH(CH₃)C(O)OCH₂CH₃][3,4-methylenedioxyphenyl], -P(O)[-N(H)C(CH₃)₂C(O)OCH₂CH₃][3,4-methylenedioxyphenyl], and -P(O)[-OCH(3-chlorophenyl)CH₂CH₂O-].

38. The compound of claim 21 wherein G is selected from the group consisting of -O- and -CH₂-; T is -CH₂CH₂-; R¹ and R² are each independently selected from the group consisting of iodo, bromo, chloro, methyl, and cyano; R⁴ is selected from the group consisting of hydrogen and iodo; R⁵ is selected from the group consisting of -OH, and -OC(O)R^e; and R³ is selected from the group consisting of iodo, bromo, optionally substituted C₁-C₆ alkyl, optionally substituted -CH₂aryl, optionally substituted -CH(OH)aryl, -C(O)-amido, -S(=O)₂-amido, wherein the amido group is selected from the group consisting of phenethylamino, piperidinyl, 4-methylpiperizinyl, morpholinyl, cyclohexylamino, aniliny, and indolinyl, and -SO₂R^e wherein R^e is selected from the group consisting of phenyl, 4-chlorophenyl, 4-fluorophenyl, and 4-pyridyl.

39. The compound of claim 38 wherein G is -O-; R¹ and R² are each chloro; R⁴ is hydrogen; R⁵ is -OH; and R³ is *iso*-propyl.

40. The compound of claim 39 wherein X is selected from the group consisting of -PO₃H₂, -P(O)[-OCH₂OC(O)-*t*-butyl]₂, -P(O)[-OCH₂OC(O)O-*i*-propyl]₂, -P(O)[-N(H)CH(CH₃)C(O)OCH₂CH₃]₂, -P(O)[-N(H)C(CH₃)₂C(O)OCH₂CH₃]₂, -P(O)[-N(H)CH(CH₃)C(O)OCH₂CH₃][3,4-methylenedioxyphenyl],

-P(O)[-N(H)C(CH₃)₂C(O)OCH₂CH₃][3,4-methylenedioxyphenyl],
and -P(O)[-OCH(3-chlorophenyl)CH₂CH₂O-].

41. The compound of claim 23 wherein T is -CH₂CH(NH₂)-; R¹ and R² are each independently selected from the group consisting of iodo, bromo, chloro, methyl, and cyano; R⁴ is selected from the group consisting of hydrogen and halogen; R⁵ is selected from the group consisting of -OH, and -OC(O)R^e; and R³ is selected from the group consisting of halogen, optionally substituted -C₁-C₆ alkyl, optionally substituted -CH₂aryl, optionally substituted -CH(OH)aryl, -C(O)-amido, -S(=O)₂-amido, wherein the amido group is selected from the group consisting of phenethylamino, piperidinyl, 4-methylpiperiziny, morpholinyl, cyclohexylamino, aniliny, and indolinyl, and -SO₂R^e wherein R^e is selected from the group consisting of phenyl, 4-chlorophenyl, 4-fluorophenyl, and 4-pyridyl.

42. The compound of claim 41 wherein G is -O-; R¹ and R² are each iodo; R⁴ is selected from the group consisting of hydrogen and iodo; R⁵ is -OH; and R³ is iodo.

43. The compound of claim 42 wherein X is selected from the group consisting of -PO₃H₂, -P(O)[-OCH₂OC(O)-*t*-butyl]₂, -P(O)[-OCH₂OC(O)O-*i*-propyl]₂, -P(O)[N(H)CH(CH₃)C(O)OCH₂CH₃]₂, -P(O)[-N(H)C(CH₃)₂C(O)OCH₂CH₃]₂, -P(O)[-N(H)CH(CH₃)C(O)OCH₂CH₃][3,4-methylenedioxyphenyl], -P(O)[-N(H)C(CH₃)₂C(O)OCH₂CH₃][3,4-methylenedioxyphenyl], and -P(O)[-OCH(3-chlorophenyl)CH₂CH₂O-].

44. The compound of claim 23 wherein T is -N(H)C(O)-; R¹ and R² are each independently selected from the group consisting of iodo, bromo, chloro, methyl, and cyano; R⁴ is selected from the group consisting of hydrogen and iodo; R⁵ is selected from the group consisting of -OH, and -OC(O)R^e; and R³ is selected from the group consisting of iodo, bromo, optionally substituted -C₁-C₆ alkyl, optionally substituted -CH₂aryl, optionally substituted -CH(OH)aryl, -C(O)-amido, -S(=O)₂-amido, wherein the amido group is selected from the group consisting of phenethylamino, piperidinyl, 4-methylpiperiziny, morpholinyl, cyclohexylamino, aniliny, and indolinyl, and -SO₂R^e wherein R^e is selected from the group consisting of phenyl, 4-chlorophenyl, 4-fluorophenyl, and 4-pyridyl.

45. The compound of claim 44 wherein G is -O-; R¹ and R² are each methyl; R⁴ is hydrogen; R⁵ is -OH; and R³ is -CH(OH)(4-fluorophenyl).

46. The compound of claim 44 wherein X is selected from the group consisting of -PO₃H₂, -P(O)[-OCH₂OC(O)-*t*-butyl]₂, -P(O)[-OCH₂OC(O)O-*i*-propyl]₂,

-P(O)[-N(H)CH(CH₃)C(O)OCH₂CH₃]₂, -P(O)[-N(H)C(CH₃)₂C(O)OCH₂CH₃]₂,
 -P(O)[-N(H)CH(CH₃)C(O)OCH₂CH₃][3,4-methylenedioxyphenyl],
 -P(O)[-N(H)C(CH₃)₂C(O)OCH₂CH₃][3,4-methylenedioxyphenyl],
 and -P(O) [-OCH(3-chlorophenyl)CH₂CH₂O-].

- 5 47. The compound of claim 23 wherein T is -OCH₂-; R¹ and R² are each independently selected from the group consisting of iodo, bromo, chloro, methyl, and cyano; R⁴ is selected from the group consisting of hydrogen and iodo; R⁵ is selected from the group consisting of -OH, and -OC(O)R^e; and R³ is selected from the group consisting of iodo, bromo, optionally substituted C₁-C₆ alkyl, optionally substituted -CH₂aryl, 10 optionally substituted -CH(OH)aryl, -C(O)-amido, -S(=O)₂-amido, wherein the amido group is selected from the group consisting of phenethylamino, piperidinyl, 4-methylpiperizinyl, morpholinyl, cyclohexylamino, anilinyl, and indolinyl, and -SO₂R^e wherein R^e is selected from the group consisting of phenyl, 4-chlorophenyl, 4-fluorophenyl, and 4-pyridyl.

- 15 48. The compound of claim 47 wherein G is -CH₂-; R¹ and R² are each methyl; R⁴ is hydrogen; R⁵ is -OH; and R³ is *iso*-propyl.

49. The compound of claim 47 wherein X is selected from the group consisting of -PO₃H₂, -P(O)[-OCH₂OC(O)-*t*-butyl]₂,
 -P(O)[-OCH₂OC(O)O-*i*-propyl]₂, -P(O)[-N(H)CH(CH₃)C(O)OCH₂CH₃]₂,
 20 -P(O)[-N(H)C(CH₃)₂C(O)OCH₂CH₃]₂,
 -P(O)[-N(H)CH(CH₃)C(O)OCH₂CH₃][3,4-methylenedioxyphenyl],
 -P(O)[-N(H)C(CH₃)₂C(O)OCH₂CH₃][3,4-methylenedioxyphenyl],
 and -P(O)[-OCH(3-chlorophenyl)CH₂CH₂O-].

50. The compound of claim 23 wherein T is -CH₂-; R¹ and R² are each 25 independently selected from the group consisting of iodo, bromo, chloro, methyl, and cyano; R⁴ is selected from the group consisting of hydrogen and iodo; R⁵ is selected from the group consisting of -OH and -OC(O)R^e; and R³ is selected from the group consisting of iodo, bromo, optionally substituted C₁-C₆ alkyl, optionally substituted -CH₂aryl, optionally substituted -CH(OH)aryl, -C(O)-amido, -S(=O)₂-amido, wherein the amido 30 group is selected from the group consisting of phenethylamino, piperidinyl, 4-methylpiperizinyl, morpholinyl, cyclohexylamino, anilinyl, and indolinyl, and -SO₂R^e wherein R^e is selected from the group consisting of phenyl, 4-chlorophenyl, 4-fluorophenyl, and 4-pyridyl.

51. The compound of claim 50 wherein when G is -O-, T is -CH₂-, R¹ and R² are independently selected from the group consisting of iodo, bromo, chloro, and methyl, R³ is alkyl of 1 to 4 carbons or cycloalkyl of 3 to 6 carbons, and R⁵ is -OH, then R⁴ is not hydrogen.

5 52. The compound of claim 50 wherein G is -O-; T is -CH₂-; R¹ and R² are each chloro; R⁴ is hydrogen; R⁵ is -OH; and R³ is *i*-propyl.

53. The compound of claim 50 wherein X is selected from the group consisting of -PO₃H₂, -P(O)[-OCH₂OC(O)-*t*-butyl]₂, -P(O)[-OCH₂OC(O)O-*i*-propyl]₂,
-P(O)[-N(H)CH(CH₃)C(O)OCH₂CH₃]₂, -P(O)[-N(H)C(CH₃)₂C(O)OCH₂CH₃]₂,
10 -P(O)[-N(H)CH(CH₃)C(O)OCH₂CH₃][3,4-methylenedioxyphenyl],
-P(O)[-N(H)C(CH₃)₂C(O)OCH₂CH₃][3,4-methylenedioxyphenyl],
and -P(O)[-OCH(3-chlorophenyl)CH₂CH₂O-].

54. The compound of claim 23 wherein T is -CH₂CH₂-; R¹ and R² are each independently selected from the group consisting of iodo, bromo, chloro, methyl, and
15 cyano; R⁴ is selected from the group consisting of hydrogen and iodo; R⁵ is selected from the group consisting of -OH and -OC(O)R^e; and R³ is selected from the group consisting of iodo, bromo, optionally substituted C₁-C₆ alkyl, optionally substituted -CH₂aryl, optionally substituted -CH(OH)aryl, -C(O)-amido, -S(=O)₂-amido, wherein the amido group is selected from the group consisting of phenethylamino, piperidinyl,
20 4-methylpiperiziny, morpholinyl, cyclohexylamino, aniliny, and indolinyl, wherein the amido group is selected from the group consisting of phenethylamino, piperidinyl, 4-methylpiperiziny, morpholinyl, cyclohexylamino, aniliny, and indolinyl, and -SO₂R^e wherein R^e is selected from the group consisting of phenyl, 4-chlorophenyl, 4-fluorophenyl, and 4-pyridyl.

25 55. The compound of claim 54 wherein when G is -O-, R¹ and R² are independently selected from the group consisting of iodo, bromo, chloro, and methyl; R³ is alkyl of 1 to 4 carbons or cycloalkyl of 3 to 6 carbons; and R⁵ is -OH; then R⁴ is not hydrogen.

56. The compound of claim 54 wherein G is -O-; T is -CH₂CH₂-; R¹ and R² are each chloro; R⁴ is hydrogen; R⁵ is -OH; and R³ is *iso*-propyl.

57. The compound of claim 54 wherein X is selected from the group consisting of -PO₃H₂, -P(O)[-OCH₂OC(O)-*t*-butyl]₂, -P(O)[-OCH₂OC(O)O-*i*-propyl]₂,
-P(O)[-N(H)CH(CH₃)C(O)OCH₂CH₃]₂, -P(O)[-N(H)C(CH₃)₂C(O)OCH₂CH₃]₂,
-P(O)[-N(H)CH(CH₃)C(O)OCH₂CH₃][3,4-methylenedioxyphenyl],

-P(O)[-N(H)C(CH₃)₂C(O)OCH₂CH₃][3,4-methylenedioxyphenyl],
and -P(O)[-OCH(3-chlorophenyl)CH₂CH₂O-].

58. The compound as in any of claims 1, 2, 3, 4, 21, 23, 25, 27, 28, 30, 31, 33, 34, 37, 38, 40, 41, 43, 44, 46, 47, 49, 50, 53, 54, or 57, wherein X is -PO₃H₂.

59. The compound of claim 32 wherein X is selected from the group consisting of -P(O)[-OCH₂OC(O)-*i*-butyl]₂ and -P(O)[-OCH₂OC(O)-*i*-propyl]₂.

60. The compound of claim 32 wherein X is selected from the group consisting of -P(O)[-OCH₂OC(O)O-ethyl]₂ and -P(O)[-OCH₂OC(O)O-*i*-propyl]₂.

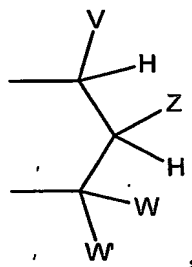
61. The compound of claim 32 wherein X is selected from the group consisting of -P(O)[-N(H)CH(CH₃)C(O)OCH₂CH₃]₂
and -P(O)[-N(H)C(CH₃)₂C(O)OCH₂CH₃]₂.

62. The compound of claim 32 wherein X is -P(O)[-OCH₂CH₂SC(O)Me]₂.

63. The compound of claim 32 wherein X is selected from the group consisting of -P(O)[-N(H)CH(CH₃)C(O)OCH₂CH₃][3,4-methylenedioxyphenyl]
and -P(O)[-N(H)C(CH₃)₂C(O)OCH₂CH₃][3,4-methylenedioxyphenyl].

64. The compound of claim 32 wherein X is -P(O)YR¹¹Y'R¹¹

wherein Y and Y' are each independently selected from -O- and -NR^v-; together R¹¹ and R¹¹ are the group:



20 wherein

V, W, and W' are independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted aralkyl, heterocycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, optionally substituted 1-alkenyl, and optionally substituted 1-alkynyl;

25 or together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 atoms, wherein 0-1 atoms are heteroatoms and the remaining atoms are carbon, substituted with hydroxy, acyloxy, alkylthiocarbonyloxy,

alkoxycarbonyloxy, or aryloxycarbonyloxy attached to a carbon atom that is three atoms from both Y groups attached to the phosphorus; or

or together V and Z are connected via an additional 3-5 atoms to form a cyclic group, wherein 0-1 atoms are heteroatoms and the remaining atoms are carbon, that is fused to an aryl group at the beta and gamma position to the Y attached to the phosphorus;

or together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to one of said carbon atoms that is three atoms from a Y attached to the phosphorus;

or together Z and W are connected via an additional 3-5 atoms to form a cyclic group, wherein 0-1 atoms are heteroatoms and the remaining atoms are carbon, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

or together W and W' are connected via an additional 2-5 atoms to form a cyclic group, wherein 0-2 atoms are heteroatoms and the remaining atoms are carbon, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

Z is selected from the group consisting of $-\text{CHR}^Z\text{OH}$, $-\text{CHR}^Z\text{OC(O)R}^Y$, $-\text{CHR}^Z\text{OC(S)R}^Y$, $-\text{CHR}^Z\text{OC(S)OR}^Y$, $-\text{CHR}^Z\text{OC(O)SR}^Y$, $-\text{CHR}^Z\text{OCO}_2\text{R}^Y$, $-\text{OR}^Z$, $-\text{SR}^Z$, $-\text{CHR}^Z\text{N}_3$, $-\text{CH}_2\text{aryl}$, $-\text{CH(aryl)OH}$, $-\text{CH(CH=CR}^Z_2\text{)OH}$, $-\text{CH(C}\equiv\text{CR}^Z\text{)OH}$, $-\text{R}^Z$, $-\text{NR}^Z_2$, $-\text{OCOR}^Y$, $-\text{OCO}_2\text{R}^Y$, $-\text{SCOR}^Y$, $-\text{SCO}_2\text{R}^Y$, $-\text{NHCOR}^Z$, $-\text{NHCO}_2\text{R}^Y$, $-\text{CH}_2\text{NHaryl}$, $-(\text{CH}_2)_q-\text{OR}^Z$, and $-(\text{CH}_2)_q-\text{SR}^Z$;

q is an integer 2 or 3;

with the provisos that:

- a) V, Z, W, W' are not all -H; and
- b) when Z is $-\text{R}^Z$, then at least one of V, W, and W' is not -H, alkyl, aralkyl, or heterocycloalkyl;

Each R^Z is selected from the group consisting of R^Y and -H;

Each R^Y is selected from the group consisting of alkyl, aryl, heterocycloalkyl, and aralkyl; and

Each R^Y is selected from the group consisting of -H, lower alkyl, acyloxyalkyl, alkoxycarbonyloxyalkyl, and lower acyl.

65. The compound of claim 64 wherein V is aryl.

66. The compound of claim 65 wherein Z is hydrogen, W is hydrogen, and W' is hydrogen.

67. The compound of claim 66 wherein V is selected from the group consisting of 3-chlorophenyl, 4-chlorophenyl, 3-bromophenyl, 3-fluorophenyl, pyrid-4-yl, pyrid-3-yl and 3,5-dichlorophenyl.

68. The compound of claim 67 wherein the relative stereochemistry between the V-group substituent and T on the dioxaphosphonane ring is *cis*.

69. The compound of claim 68 wherein said *cis* dioxaphosphonane ring has *R* stereochemistry at the carbon where the V-group is attached.

70. The compound of claim 68 wherein said *cis* dioxaphosphonane ring has *S* stereochemistry at the carbon where the V-group is attached.

71. The compound of claim 19 wherein G is -O-, T is -CH₂CH₂-, R¹ and R² are each iodo, and R³ is *iso*-propyl, R⁴ is hydrogen, and R⁵ is -OH.

72. The compound of claim 71 wherein X is selected from the group consisting of -P(O)[-OCH(V)CH₂CH₂O-], -P(O)[-N(H)CH(CH₃)C(O)OCH₂CH₃]₂, and -P(O)[-N(H)C(CH₃)₂C(O)OCH₂CH₃]₂, and V is selected from the group consisting of aryl, substituted aryl, heteroaryl, and substituted heteroaryl.

73. The compound of claim 19 wherein G is -O-, T is -CH₂CH₂-, R¹, R² and R³ are each iodo, R⁴ is hydrogen, and R⁵ is -OH.

74. The compound of claim 73 wherein X is selected from the group consisting of -P(O)[-OCH(V)CH₂CH₂O-], -P(O)[-N(H)CH(CH₃)C(O)OCH₂CH₃]₂, and -P(O)[-N(H)C(CH₃)₂C(O)OCH₂CH₃]₂, and V is selected from the group consisting of aryl, substituted aryl, heteroaryl, and substituted heteroaryl.

75. The compound of claim 19 wherein G is -O-, T is -CH₂-, R¹ and R² are each iodo, R³ is *iso*-propyl, R⁴ is hydrogen, and R⁵ is -OH.

76. The compound of claim 75 wherein X is selected from the group consisting of -P(O)[-OCH(V)CH₂CH₂O-], -P(O)[-N(H)CH(CH₃)C(O)OCH₂CH₃]₂, and -P(O)[-N(H)C(CH₃)₂C(O)OCH₂CH₃]₂, and V is selected from the group consisting of aryl, substituted aryl, heteroaryl, and substituted heteroaryl.

77. The compound of claim 19 wherein G is -O-, T is -CH₂-, R¹, R² and R³ are each iodo, R⁴ is hydrogen, and R⁵ is -OH.

78. The compound of claim 77 wherein X is selected from the group consisting of -P(O)[-OCH(V)CH₂CH₂O-], -P(O)[-N(H)CH(CH₃)C(O)OCH₂CH₃]₂,

and $-P(O)[-N(H)C(CH_3)_2C(O)OCH_2CH_3]_2$, and V is selected from the group consisting of aryl, substituted aryl, heteroaryl, and substituted heteroaryl.

79. The compound of claim 19 wherein G is -O-, T is $-OCH_2-$, R^1 and R^2 are each iodo, and R^3 is *iso*-propyl, R^4 is hydrogen, and R^5 is -OH.

5 80. The compound of claim 79 wherein X is selected from the group consisting of $-P(O)[-OCH(V)CH_2CH_2O-]$, $-P(O)[-N(H)CH(CH_3)C(O)OCH_2CH_3]_2$, and $-P(O)[-N(H)C(CH_3)_2C(O)OCH_2CH_3]_2$, and V is selected from the group consisting of aryl, substituted aryl, heteroaryl, and substituted heteroaryl.

10 81. The compound of claim 19 wherein G is -O-, T is $-CH_2-$, R^1 and R^2 are each chloro, R^3 is 4-fluorobenzyl, R^4 is hydrogen, and R^5 is -OH.

82. The compound of claim 81 wherein X is selected from the group consisting of $-P(O)[-OCH(V)CH_2CH_2O-]$, $-P(O)[-N(H)CH(CH_3)C(O)OCH_2CH_3]_2$, and $-P(O)[-N(H)C(CH_3)_2C(O)OCH_2CH_3]_2$, and V is selected from the group consisting of aryl, substituted aryl, heteroaryl, and substituted heteroaryl.

15 83. A method of preventing or treating a metabolic disease comprising administering to an animal a pharmaceutically effective amount of a phosphonic acid-containing compound, a pharmaceutically acceptable salt thereof, or prodrugs thereof or pharmaceutically acceptable salts of said prodrugs, wherein said phosphonic acid containing compound binds to a thyroid receptor.

20 84. The method of claim 83 wherein said phosphonic acid containing-compound binds to a thyroid receptor with a K_i of $\leq 1 \mu M$.

85. The method of claim 84 wherein said thyroid receptor is $TR\alpha 1$.

86. The method of claim 84 wherein said thyroid receptor is $TR\beta 1$.

25 87. The method of claim 84 wherein said phosphonic acid-containing compound binds to a thyroid receptor with a K_i of $\leq 100 \text{ nM}$.

88. The method of claim 87 wherein said thyroid receptor is $TR\alpha 1$.

89. The method of claim 87 wherein said thyroid receptor is $TR\beta 1$.

30 90. The method of claim 83 wherein said metabolic disease is selected from the group consisting of obesity, hypercholesterolemia, hyperlipidemia, atherosclerosis, coronary heart disease, and hypertension.

91. The method of claim 90 wherein said metabolic disease is selected from the group consisting of obesity, hypercholesterolemia, and hyperlipidemia.

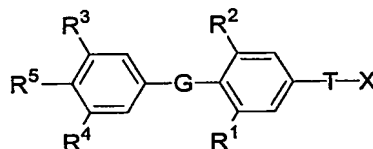
92. The method of claim 83, wherein said phosphonic acid-containing compound activates said thyroid receptor.

93. The method of claim 92 wherein said thyroid receptor is TR α 1.

94. The method of claim 92 wherein said thyroid receptor is TR β 1.

5 95. The method of claim 91 wherein said phosphonic acid containing-compound increases mRNA expression of a gene selected from the group consisting of LDL receptor, ACC, FAS, spot-14, CPT-1, CYP7A, apo AI, and mGPDH.

96. The method of claim 83 wherein said phosphonic acid-containing compound is a compound of Formula I:



10

wherein:

G is selected from the group consisting of -O-, -S-, -S(=O)-, -S(=O)₂-, -CH₂-, -CF₂-, -CHF-, -C(O)-, -CH(OH)-, -NH-, and -N(C₁-C₄ alkyl)-;

15 T is selected from the group consisting of -(CR^a)_k-, -CR^b=CR^b-(CR^a)_n-, -(CR^a)_n-CR^b=CR^b-, -(CR^a)₂-CR^b=CR^b-(CR^a)₂-, -O(CR^b)₂(CR^a)_n-, -S(CR^b)₂(CR^a)_n-, -N(R^c)(CR^b)₂(CR^a)_n-, -N(R^b)C(O)(CR^a)_n-, -(CR^a)_nCH(NR^bR^c)-, -C(O)(CR^a)_m-, -(CR^a)_mC(O)-, -(CR^a)C(O)(CR^a)_n-, -(CR^a)_nC(O)(CR^a)₂-, and -C(O)NH(CR^b)₂(CR^a)_p-;

k is an integer from 0-4;

20 m is an integer from 0-3;

n is an integer from 0-2;

p is an integer from 0-1;

25 Each R^a is independently selected from the group consisting of hydrogen, optionally substituted -C₁-C₄ alkyl, halogen, -OH, optionally substituted -O-C₁-C₄ alkyl, -OCF₃, optionally substituted -S-C₁-C₄ alkyl, -NR^bR^c, optionally substituted -C₂-C₄ alkenyl, and optionally substituted -C₂-C₄ alkynyl; with the proviso that when one R^a is attached to C through an O, S, or N atom, then the other R^a attached to the same C is a hydrogen, or attached via a carbon atom;

30 Each R^b is independently selected from the group consisting of hydrogen and optionally substituted -C₁-C₄ alkyl;

Each R^c is independently selected from the group consisting of hydrogen and optionally substituted $-C_1-C_4$ alkyl, optionally substituted $-C(O)-C_1-C_4$ alkyl, and $-C(O)H$;

R^1 and R^2 are each independently selected from the group consisting of halogen, optionally substituted $-C_1-C_4$ alkyl, optionally substituted $-S-C_1-C_3$ alkyl, optionally substituted $-C_2-C_4$ alkenyl, optionally substituted $-C_2-C_4$ alkynyl, $-CF_3$, $-OCF_3$, optionally substituted $-O-C_1-C_3$ alkyl, and cyano;

R^3 and R^4 are each independently selected from the group consisting of hydrogen, halogen, $-CF_3$, $-OCF_3$, cyano, optionally substituted $-C_1-C_{12}$ alkyl, optionally substituted $-C_2-C_{12}$ alkenyl, optionally substituted $-C_2-C_{12}$ alkynyl, optionally substituted $-(CR^a_2)_m$ aryl, optionally substituted $-(CR^a_2)_m$ cycloalkyl, optionally substituted $-(CR^a_2)_m$ heterocycloalkyl, $-OR^d$, $-SR^d$, $-S(=O)R^e$, $-S(=O)_2R^e$, $-S(=O)_2NR^fR^g$, $-C(O)NR^fR^g$, $-C(O)OR^h$, $-C(O)R^e$, $-N(R^b)C(O)R^e$, $-N(R^b)C(O)NR^fR^g$, $-N(R^b)S(=O)_2R^e$, $-N(R^b)S(=O)_2NR^fR^g$, and $-NR^fR^g$;

Each R^d is selected from the group consisting of optionally substituted $-C_1-C_{12}$ alkyl, optionally substituted $-C_2-C_{12}$ alkenyl, optionally substituted $-C_2-C_{12}$ alkynyl, optionally substituted $-(CR^b_2)_n$ aryl, optionally substituted $-(CR^b_2)_n$ cycloalkyl, optionally substituted $-(CR^b_2)_n$ heterocycloalkyl, and $-C(O)NR^fR^g$;

Each R^e is selected from the group consisting of optionally substituted $-C_1-C_{12}$ alkyl, optionally substituted $-C_2-C_{12}$ alkenyl, optionally substituted $-C_2-C_{12}$ alkynyl, optionally substituted $-(CR^a_2)_n$ aryl, optionally substituted $-(CR^a_2)_n$ cycloalkyl, and optionally substituted $-(CR^a_2)_n$ heterocycloalkyl;

R^f and R^g are each independently selected from the group consisting of hydrogen, optionally substituted $-C_1-C_{12}$ alkyl, optionally substituted $-C_2-C_{12}$ alkenyl, optionally substituted $-C_2-C_{12}$ alkynyl, optionally substituted $-(CR^b_2)_n$ aryl, optionally substituted $-(CR^b_2)_n$ cycloalkyl, and optionally substituted $-(CR^b_2)_n$ heterocycloalkyl, or R^f and R^g may together form an optionally substituted heterocyclic ring, which may contain a second heterogroup selected from the group consisting of O, NR^c , and S, wherein said optionally substituted heterocyclic ring may be substituted with 0-4 substituents selected from the group consisting of optionally substituted $-C_1-C_4$ alkyl, $-OR^b$, oxo, cyano, $-CF_3$, optionally substituted phenyl, and $-C(O)OR^h$;

Each R^h is selected from the group consisting of optionally substituted $-C_1-C_{12}$ alkyl, optionally substituted $-C_2-C_{12}$ alkenyl, optionally substituted $-C_2-C_{12}$ alkynyl,

optionally substituted $-(CR^b)_n$ aryl, optionally substituted $-(CR^b)_n$ cycloalkyl, and optionally substituted $-(CR^b)_n$ heterocycloalkyl;

R^5 is selected from the group consisting of -OH, optionally substituted $-OC_1-C_6$ alkyl, $-OC(O)R^e$, $-OC(O)OR^h$, -F, $-NHC(O)R^e$, $-NHS(=O)R^e$, $-NHS(=O)_2R^e$,
 5 $-NHC(=S)NH(R^h)$, and $-NHC(O)NH(R^h)$;

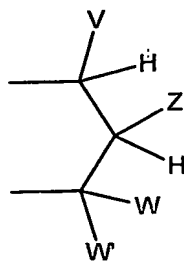
X is $P(O)YR^{11}Y'R^{11}$;

Y and Y' are each independently selected from the group consisting of -O-, and $-NR^v$ -; when Y and Y' are -O-, R^{11} attached to -O- is independently selected from the group consisting of -H, alkyl, optionally substituted aryl, optionally substituted
 10 heterocycloalkyl, optionally substituted CH_2 -heterocycloalkyl wherein the cyclic moiety contains a carbonate or thiocarbonate, optionally substituted -alkylaryl, $-C(R^z)_2OC(O)NR^z$, $-NR^z-C(O)-R^y$, $-C(R^z)_2-OC(O)R^y$, $-C(R^z)_2-O-C(O)OR^y$, $-C(R^z)_2OC(O)SR^y$, -alkyl-S-C(O) R^y , -alkyl-S-S-alkylhydroxy, and -alkyl-S-S-S-alkylhydroxy;

15 when Y and Y' are $-NR^v$ -, then R^{11} attached to $-NR^v$ - is independently selected from the group consisting of -H, $-[C(R^z)_2]_q-COOR^y$, $-C(R^x)_2COOR^y$, $-[C(R^z)_2]_q-C(O)SR^y$, and -cycloalkylene- $COOR^y$;

when Y is -O- and Y' is NR^v , then R^{11} attached to -O- is independently selected
 20 from the group consisting of -H, alkyl, optionally substituted aryl, optionally substituted heterocycloalkyl, optionally substituted CH_2 -heterocycloalkyl wherein the cyclic moiety contains a carbonate or thiocarbonate, optionally substituted -alkylaryl, $-C(R^z)_2OC(O)NR^z$, $-NR^z-C(O)-R^y$, $-C(R^z)_2-OC(O)R^y$, $-C(R^z)_2-O-C(O)OR^y$, $-C(R^z)_2OC(O)SR^y$, -alkyl-S-C(O) R^y , -alkyl-S-S-alkylhydroxy,
 25 and -alkyl-S-S-S-alkylhydroxy; and R^{11} attached to $-NR^v$ - is independently selected from the group consisting of -H, $-[C(R^z)_2]_q-COOR^y$, $-C(R^x)_2COOR^y$, $-[C(R^z)_2]_q-C(O)SR^y$, and -cycloalkylene- $COOR^y$;

or when Y and Y' are independently selected from -O- and $-NR^v$ -, then together R^{11} and R^{11} are -alkyl-S-S-alkyl- to form a cyclic group, or together R^{11} and R^{11} are the
 30 group:



wherein:

V, W, and W' are independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted aralkyl, heterocycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, optionally substituted 1-alkenyl, and optionally substituted 1-alkynyl;

or together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 atoms, wherein 0-1 atoms are heteroatoms and the remaining atoms are carbon, substituted with hydroxy, acyloxy, alkylthiocarbonyloxy, alkoxycarbonyloxy, or aryloxy carbonyloxy attached to a carbon atom that is three atoms from both Y groups attached to the phosphorus; or

or together V and Z are connected via an additional 3-5 atoms to form a cyclic group, wherein 0-1 atoms are heteroatoms and the remaining atoms are carbon, that is fused to an aryl group at the beta and gamma position to the Y attached to the phosphorus;

or together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxy carbonyloxy, attached to one of said carbon atoms that is three atoms from a Y attached to the phosphorus;

or together Z and W are connected via an additional 3-5 atoms to form a cyclic group, wherein 0-1 atoms are heteroatoms and the remaining atoms are carbon, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

or together W and W' are connected via an additional 2-5 atoms to form a cyclic group, wherein 0-2 atoms are heteroatoms and the remaining atoms are carbon, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

Z is selected from the group consisting of $-\text{CHR}^z\text{OH}$, $-\text{CHR}^z\text{OC(O)R}^y$, $-\text{CHR}^z\text{OC(S)R}^y$, $-\text{CHR}^z\text{OC(S)OR}^y$, $-\text{CHR}^z\text{OC(O)SR}^y$, $-\text{CHR}^z\text{OCO}_2\text{R}^y$, $-\text{OR}^z$,

-SR^z, -CHR^zN₃, -CH₂aryl, -CH(aryl)OH, -CH(CH=CR^z)OH, -CH(C≡CR^z)OH, -R^z, -NR^z, -OCOR^y, -OCO₂R^y, -SCOR^y, -SCO₂R^y, -NHCOR^z, -NHCO₂R^y, -CH₂NHaryl, -(CH₂)_q-OR^z, and -(CH₂)_q-SR^z;

q is an integer 2 or 3;

5 Each R^z is selected from the group consisting of R^y and -H;

Each R^y is selected from the group consisting of alkyl, aryl, heterocycloalkyl, and aralkyl;

Each R^x is independently selected from the group consisting of -H, and alkyl, or together R^x and R^x form a cyclic alkyl group;

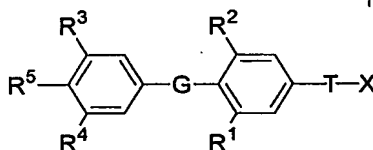
10 Each R^v is selected from the group consisting of -H, lower alkyl, acyloxyalkyl, alkoxy-carbonyloxyalkyl, and lower acyl;

with the provisos that:

- a) when G is -O-, T is -CH₂-, R¹ and R² are each bromo, R³ is *iso*-propyl, R⁴ is hydrogen, and R⁵ is -OH, then X is not P(O)(OH)₂ or P(O)(OCH₂CH₃)₂;
- 15 b) V, Z, W, W' are not all -H; and
- c) when Z is -R^z, then at least one of V, W, and W' is not -H, alkyl, aralkyl, or heterocycloalkyl;

and pharmaceutically acceptable salts and prodrugs thereof and pharmaceutically acceptable salts of said prodrugs.

20 97. The method of claim 83 wherein said phosphonic acid-containing compound is a compound of Formula I:



wherein:

- G is selected from the group consisting of -O-, -S-, -S(=O)-, -S(=O)₂-,
- 25 -CH₂-, -CF₂-, -CHF-, -C(O)-, -CH(OH)-, -NH-, and -N(C₁-C₄ alkyl)-;
- T is selected from the group consisting of -(CR^a)_k-, -CR^b=CR^b-(CR^a)_n-, -(CR^a)_n-CR^b=CR^b-, -(CR^a)₂-CR^b=CR^b-(CR^a)₂-, -O(CR^b)₂(CR^a)_n-, -S(CR^b)₂(CR^a)_n-, -N(R^c)(CR^b)₂(CR^a)_n-, -N(R^b)C(O)(CR^a)_n-, -(CR^a)_nCH(NR^bR^c)-, -C(O)(CR^a)_m-, -(CR^a)_mC(O)-, -(CR^a)C(O)(CR^a)_n-,
- 30 -(CR^a)_nC(O)(CR^a)₂-, and -C(O)NH(CR^b)₂(CR^a)_p-;

k is an integer from 0-4;

m is an integer from 0-3;

n is an integer from 0-2;

p is an integer from 0-1;

- 5 Each R^a is independently selected from the group consisting of hydrogen, optionally substituted -C₁-C₄ alkyl, halogen, -OH, optionally substituted -O-C₁-C₄ alkyl, -OCF₃, optionally substituted -S-C₁-C₄ alkyl, -NR^bR^c, optionally substituted -C₂-C₄ alkenyl, and optionally substituted -C₂-C₄ alkynyl; with the proviso that when one R^a is attached to C through an O, S, or N atom, then the other R^a attached
10 to the same C is a hydrogen, or attached via a carbon atom;

Each R^b is independently selected from the group consisting of hydrogen and optionally substituted -C₁-C₄ alkyl;

- Each R^c is independently selected from the group consisting of hydrogen, optionally substituted -C₁-C₄ alkyl, optionally substituted -C(O)-C₁-C₄ alkyl,
15 and -C(O)H;

R¹ and R² are each independently selected from the group consisting of halogen, optionally substituted -C₁-C₄ alkyl, optionally substituted -S-C₁-C₃ alkyl, optionally substituted -C₂-C₄ alkenyl, optionally substituted -C₂-C₄ alkynyl, -CF₃, -OCF₃, optionally substituted -O-C₁-C₃ alkyl, and cyano;

- 20 R³ and R⁴ are each independently selected from the group consisting of hydrogen, halogen, -CF₃, -OCF₃, cyano, optionally substituted -C₁-C₁₂ alkyl, optionally substituted -C₂-C₁₂ alkenyl, optionally substituted -C₂-C₁₂ alkynyl, optionally substituted -(CR^a)_maryl, optionally substituted -(CR^a)_mcycloalkyl, optionally substituted (CR^a)_mheterocycloalkyl, -OR^d, -SR^d, -S(=O)R^e, -S(=O)₂R^e, -S(=O)₂NR^fR^g, -C(O)NR^fR^g,
25 , -C(O)OR^h, -C(O)R^e, -N(R^b)C(O)R^e, -N(R^b)C(O)NR^fR^g, -N(R^b)S(=O)₂R^e, -N(R^b)S(=O)₂NR^fR^g, and -NR^fR^g;

- Each R^d is selected from the group consisting of optionally substituted -C₁-C₁₂ alkyl, optionally substituted -C₂-C₁₂ alkenyl, optionally substituted -C₂-C₁₂ alkynyl, optionally substituted -(CR^b)_naryl, optionally substituted -(CR^b)_ncycloalkyl, optionally substituted -(CR^b)_nheterocycloalkyl, and -C(O)NR^fR^g;
30

Each R^e is optionally substituted -C₁-C₁₂ alkyl, optionally substituted -C₂-C₁₂ alkenyl, optionally substituted -C₂-C₁₂ alkynyl, optionally substituted -(CR^a)_naryl, optionally substituted -(CR^a)_ncycloalkyl, and optionally substituted -(CR^a)_nheterocycloalkyl;

R^f and R^g are each independently selected from the group consisting of hydrogen, optionally substituted $-C_1-C_{12}$ alkyl, optionally substituted $-C_2-C_{12}$ alkenyl, optionally substituted $-C_2-C_{12}$ alkynyl, optionally substituted $-(CR^b)_n$ aryl, optionally substituted $-(CR^b)_n$ cycloalkyl, and optionally substituted $-(CR^b)_n$ heterocycloalkyl, or R^f and R^g may together form an optionally substituted heterocyclic ring, which may contain a second heterogroup selected from the group of O, NR^c , and S, wherein said optionally substituted heterocyclic ring may be substituted with 0-4 substituents selected from the group consisting of optionally substituted $-C_1-C_4$ alkyl, $-OR^b$, oxo, cyano, $-CF_3$, optionally substituted phenyl, and $-C(O)OR^h$;

Each R^h is selected from the group consisting of optionally substituted $-C_1-C_{12}$ alkyl, optionally substituted $-C_2-C_{12}$ alkenyl, optionally substituted $-C_2-C_{12}$ alkynyl, optionally substituted $-(CR^b)_n$ aryl, optionally substituted $-(CR^b)_n$ cycloalkyl, and optionally substituted $-(CR^b)_n$ heterocycloalkyl;

R^5 is selected from the group consisting of $-OH$, optionally substituted $-OC_1-C_6$ alkyl, $-OC(O)R^e$, $-OC(O)OR^h$, $-F$, $-NHC(O)R^e$, $-NHS(=O)_2R^e$, $-NHS(=O)R^e$, $-NHC(=S)NH(R^h)$, and $-NHC(O)NH(R^h)$;

X is $P(O)YR^{11}Y'R^{11}$;

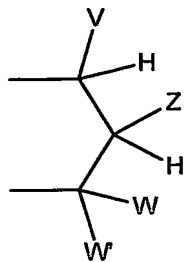
Y and Y' are each independently selected from the group consisting of $-O-$, and $-NR^v-$; when Y and Y' are $-O-$, R^{11} attached to $-O-$ is independently selected from the group consisting of $-H$, alkyl, optionally substituted aryl, optionally substituted heterocycloalkyl, optionally substituted CH_2 -heterocycloalkyl wherein the cyclic moiety contains a carbonate or thiocarbonate, optionally substituted $-alkylaryl$, $-C(R^z)_2OC(O)NR^z$, $-NR^z-C(O)-R^y$, $-C(R^z)_2-OC(O)R^y$, $-C(R^z)_2-O-C(O)OR^y$, $-C(R^z)_2OC(O)SR^y$, $-alkyl-S-C(O)R^y$, $-alkyl-S-S-alkylhydroxy$, and $-alkyl-S-S-S-alkylhydroxy$;

when Y and Y' are $-NR^v-$, then R^{11} attached to $-NR^v-$ is independently selected from the group consisting of $-H$, $-[C(R^z)_2]_q-COOR^y$, $-C(R^x)_2COOR^y$, $-[C(R^z)_2]_q-C(O)SR^y$, and $-cycloalkylene-COOR^y$;

when Y is $-O-$ and Y' is NR^v , then R^{11} attached to $-O-$ is independently selected from the group consisting of $-H$, alkyl, optionally substituted aryl, optionally substituted heterocycloalkyl, optionally substituted CH_2 -heterocycloalkyl wherein the cyclic moiety contains a carbonate or thiocarbonate, optionally substituted $-alkylaryl$, $-C(R^z)_2OC(O)NR^z$, $-NR^z-C(O)-R^y$, $-C(R^z)_2-OC(O)R^y$,

$-C(R^z)_2-O-C(O)OR^y$, $-C(R^z)_2OC(O)SR^y$, $-alkyl-S-C(O)R^y$, $-alkyl-S-S-alkylhydroxy$, and $-alkyl-S-S-S-alkylhydroxy$; and R^{11} attached to $-NR^y-$ is independently selected from the group consisting of $-H$, $-[C(R^z)_2]_q-COOR^y$, $-C(R^x)_2COOR^y$, $-[C(R^z)_2]_q-C(O)SR^y$, and $-cycloalkylene-COOR^y$;

- 5 or when Y and Y' are independently selected from $-O-$ and $-NR^y-$, then together R^{11} and R^{11} are $-alkyl-S-S-alkyl-$ to form a cyclic group, or together R^{11} and R^{11} are the group:



wherein:

- 10 V , W , and W' are independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted aralkyl, heterocycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, optionally substituted 1-alkenyl, and optionally substituted 1-alkynyl;

- or together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 atoms, wherein 0 – 1 atoms are heteroatoms and the remaining atoms are carbon, substituted with hydroxy, acyloxy, alkylthiocarbonyloxy, alkoxycarbonyloxy, or aryloxycarbonyloxy attached to a carbon atom that is three atoms from both Y groups attached to the phosphorus; or

- 15 or together V and Z are connected via an additional 3-5 atoms to form a cyclic group, wherein 0–1 atoms are heteroatoms and the remaining atoms are carbon, that is fused to an aryl group at the beta and gamma position to the Y attached to the phosphorus;

- 20 or together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to one of said carbon atoms that is three atoms from a Y attached to the phosphorus;

or together Z and W are connected via an additional 3-5 atoms to form a cyclic group, wherein 0-1 atoms are heteroatoms and the remaining atoms are carbon, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

or together W and W' are connected via an additional 2-5 atoms to form a cyclic group, wherein 0-2 atoms are heteroatoms and the remaining atoms are carbon, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

Z is selected from the group consisting of $-\text{CHR}^z\text{OH}$, $-\text{CHR}^z\text{OC}(\text{O})\text{R}^y$, $-\text{CHR}^z\text{OC}(\text{S})\text{R}^y$, $-\text{CHR}^z\text{OC}(\text{S})\text{OR}^y$, $-\text{CHR}^z\text{OC}(\text{O})\text{SR}^y$, $-\text{CHR}^z\text{OCO}_2\text{R}^y$, $-\text{OR}^z$, $-\text{SR}^z$, $-\text{CHR}^z\text{N}_3$, $-\text{CH}_2\text{aryl}$, $-\text{CH}(\text{aryl})\text{OH}$, $-\text{CH}(\text{CH}=\text{CR}^z_2)\text{OH}$, $-\text{CH}(\text{C}\equiv\text{CR}^z)\text{OH}$, $-\text{R}^z$, $-\text{NR}^z_2$, $-\text{OCOR}^y$, $-\text{OCO}_2\text{R}^y$, $-\text{SCOR}^y$, $-\text{SCO}_2\text{R}^y$, $-\text{NHCOR}^z$, $-\text{NHCO}_2\text{R}^y$, $-\text{CH}_2\text{NHaryl}$, $-(\text{CH}_2)_q-\text{OR}^z$, and $-(\text{CH}_2)_q-\text{SR}^z$;

q is an integer 2 or 3;

Each R^z is selected from the group consisting of R^y and $-\text{H}$;

Each R^y is selected from the group consisting of alkyl, aryl, heterocycloalkyl, and aralkyl;

Each R^x is independently selected from the group consisting of $-\text{H}$, and alkyl, or together R^x and R^x form a cyclic alkyl group;

Each R^v is selected from the group consisting of $-\text{H}$, lower alkyl, acyloxyalkyl, alkoxy-carbonyloxyalkyl, and lower acyl;

with the provisos that:

a) when G is $-\text{O}-$, T is $-(\text{CH}_2)_{0-4}-$, R^1 and R^2 are independently halogen, alkyl of 1 to 3 carbons, and cycloalkyl of 3 to 5 carbons, R^3 is alkyl of 1 to 4 carbons or cycloalkyl of 3 to 7 carbons, R^4 is hydrogen, and R^5 is $-\text{OH}$, then X is not $-\text{P}(\text{O})(\text{OH})_2$ or $-\text{P}(\text{O})(\text{O-lower alkyl})_2$;

b) when G is $-\text{O}-$, R^5 is $-\text{NHC}(\text{O})\text{R}^e$, $-\text{NHS}(=\text{O})_{1-2}\text{R}^e$, $-\text{NHC}(\text{S})\text{NH}(\text{R}^h)$, or $-\text{NHC}(\text{O})\text{NH}(\text{R}^h)$, T is $-(\text{CH}_2)_m-$, $-\text{CH}=\text{CH}-$, $-\text{O}(\text{CH}_2)_{1-2}-$, or $-\text{NH}(\text{CH}_2)_{1-2}-$, then X is not $-\text{P}(\text{O})(\text{OH})_2$ or $-\text{P}(\text{O})(\text{OH})\text{NH}_2$;

c) V, Z, W, W' are not all $-\text{H}$; and

d) when Z is $-\text{R}^z$, then at least one of V, W, and W' is not $-\text{H}$, alkyl, aralkyl, or heterocycloalkyl;

and pharmaceutically acceptable salts and prodrugs thereof and pharmaceutically acceptable salts of said prodrugs.

98. The method of claim 96 wherein when G is $-\text{O}-$, T is $-\text{CH}_2-$, R^1 and R^2 are each bromo, R^3 is *iso*-propyl, and R^5 is $-\text{OH}$, then R^4 is not hydrogen.

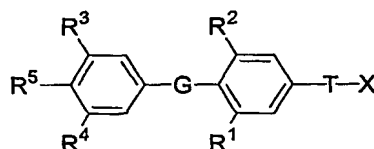
99. The method of claim 97 wherein when G is -O-, T is $-(CH_2)_0-$, R^1 and R^2 are independently selected from the group consisting of halogen, alkyl of 1 to 3 carbons, and cycloalkyl of 3 to 5 carbons, R^3 is alkyl of 1 to 4 carbons or cycloalkyl of 3 to 7 carbons, and R^5 is -OH, then R^4 is not hydrogen; and wherein when G is -O-, R^5 is selected from the group consisting of $NHC(O)R^e$, $-NHS(=O)_{1-2}R^e$, $-NHC(=S)NH(R^h)$, and $-NHC(O)NH(R^h)$, T is selected from the group consisting of $-(CH_2)_m-$, $-CH=CH-$, $-O(CH_2)_{1-2}-$, and $-NH(CH_2)_{1-2}-$, then R^4 is not hydrogen.

100. A method of activating a thyroid receptor in an animal by administering a phosphonic acid-containing-compound wherein said activation results in the 50% or greater increase in the mRNA expression of a gene selected from the group consisting of LDL receptor, ACC, FAS, spot-14, CPT-1, CYP7A, apo AI, and mGPDH.

101. The method of claim 100 wherein said phosphonic acid-containing-compound binds to a thyroid receptor with a K_i of $\leq 1 \mu M$.

102. The method of claim 101 wherein said phosphonic acid-containing-compound binds to a thyroid receptor with a K_i of ≤ 100 nM.

103. The method of claim 100 wherein said phosphonic acid-containing compound is a compound of Formula I:



wherein:

G is selected from the group consisting of -O-, -S-, $-S(=O)-$, $-S(=O)_2-$, $-CH_2-$, $-CF_2-$, $-CHF-$, $-C(O)-$, $-CH(OH)-$, $-NH-$, and $-N(C_1-C_4 \text{ alkyl})-$;

T is selected from the group consisting of $-(CR^a_2)_k-$, $-CR^b=CR^b-(CR^a_2)_n-$, $-(CR^a_2)_n-CR^b=CR^b-$, $-(CR^a_2)-CR^b=CR^b-(CR^a_2)-$, $-O(CR^b_2)(CR^a_2)_n-$, $-S(CR^b_2)(CR^a_2)_n-$, $-N(R^c)(CR^b_2)(CR^a_2)_n-$, $-N(R^b)C(O)(CR^a_2)_n-$, $-(CR^a_2)_nCH(NR^bR^c)-$, $-C(O)(CR^a_2)_m-$, $-(CR^a_2)_mC(O)-$, $-(CR^a_2)C(O)(CR^a_2)_n-$, $-(CR^a_2)_nC(O)(CR^a_2)-$, and $-C(O)NH(CR^b_2)(CR^a_2)_p-$;

k is an integer from 0-4;

m is an integer from 0-3;

n is an integer from 0-2;

p is an integer from 0-1;

Each R^a is independently selected from the group consisting of hydrogen, optionally substituted $-C_1-C_4$ alkyl, halogen, $-OH$, optionally substituted $-O-C_1-C_4$ alkyl, $-OCF_3$, optionally substituted $-S-C_1-C_4$ alkyl, $-NR^bR^c$, optionally substituted $-C_2-C_4$ alkenyl, and optionally substituted $-C_2-C_4$ alkynyl; with the proviso
 5 that when one R^a is attached to C through an O, S, or N atom, then the other R^a attached to the same C is a hydrogen, or attached via a carbon atom;

Each R^b is independently selected from the group consisting of hydrogen and optionally substituted $-C_1-C_4$ alkyl;

Each R^c is independently selected from the group consisting of hydrogen and
 10 optionally substituted $-C_1-C_4$ alkyl, optionally substituted $-C(O)-C_1-C_4$ alkyl, and $-C(O)H$;

R^1 and R^2 are each independently selected from the group consisting of halogen, optionally substituted $-C_1-C_4$ alkyl, optionally substituted $-S-C_1-C_3$ alkyl, optionally substituted $-C_2-C_4$ alkenyl, optionally substituted $-C_2-C_4$ alkynyl, $-CF_3$, $-OCF_3$, optionally
 15 substituted $-O-C_1-C_3$ alkyl, and cyano;

R^3 and R^4 are each independently selected from the group consisting of hydrogen, halogen, $-CF_3$, $-OCF_3$, cyano, optionally substituted $-C_1-C_{12}$ alkyl, optionally substituted $-C_2-C_{12}$ alkenyl, optionally substituted $-C_2-C_{12}$ alkynyl, optionally substituted $-(CR^a)_m$ aryl, optionally substituted $-(CR^a)_m$ cycloalkyl, optionally
 20 substituted $-(CR^a)_m$ heterocycloalkyl, $-OR^d$, $-SR^d$, $-S(=O)R^e$, $-S(=O)_2R^e$, $-S(=O)_2NR^fR^g$, $-C(O)NR^fR^g$, $-C(O)OR^h$, $-C(O)R^e$, $-N(R^b)C(O)R^e$, $-N(R^b)C(O)NR^fR^g$, $-N(R^b)S(=O)_2R^e$, $-N(R^b)S(=O)_2NR^fR^g$, and $-NR^fR^g$;

Each R^d is selected from the group consisting of optionally substituted $-C_1-C_{12}$ alkyl, optionally substituted $-C_2-C_{12}$ alkenyl, optionally substituted $-C_2-C_{12}$ alkynyl,
 25 optionally substituted $-(CR^b)_n$ aryl, optionally substituted $-(CR^b)_n$ cycloalkyl, optionally substituted $-(CR^b)_n$ heterocycloalkyl, and $-C(O)NR^fR^g$;

Each R^e is selected from the group consisting of optionally substituted $-C_1-C_{12}$ alkyl, optionally substituted $-C_2-C_{12}$ alkenyl, optionally substituted $-C_2-C_{12}$ alkynyl,
 30 optionally substituted $-(CR^a)_n$ aryl, optionally substituted $-(CR^a)_n$ cycloalkyl, and optionally substituted $-(CR^a)_n$ heterocycloalkyl;

R^f and R^g are each independently selected from the group consisting of hydrogen, optionally substituted $-C_1-C_{12}$ alkyl, optionally substituted $-C_2-C_{12}$ alkenyl, optionally substituted $-C_2-C_{12}$ alkynyl, optionally substituted $-(CR^b)_n$ aryl, optionally substituted $-(CR^b)_n$ cycloalkyl, and optionally substituted $-(CR^b)_n$ heterocycloalkyl, or R^f

and R^g may together form an optionally substituted heterocyclic ring, which may contain a second heterogroup selected from the group consisting of O, NR^e, and S, wherein said optionally substituted heterocyclic ring may be substituted with 0-4 substituents selected from the group consisting of optionally substituted -C₁-C₄ alkyl, -OR^b, oxo, cyano, -CF₃,
 5 optionally substituted phenyl, and -C(O)OR^h;

Each R^h is selected from the group consisting of optionally substituted -C₁-C₁₂ alkyl, optionally substituted -C₂-C₁₂ alkenyl, optionally substituted -C₂-C₁₂ alkynyl, optionally substituted -(CR^b)_naryl, optionally substituted -(CR^b)_ncycloalkyl, and optionally substituted -(CR^b)_nheterocycloalkyl;

10 R⁵ is selected from the group consisting of -OH, optionally substituted -OC₁-C₆ alkyl, -OC(O)R^e, -OC(O)OR^h, -F, -NHC(O)R^e, -NHS(=O)R^e, -NHS(=O)₂R^e, -NHC(=S)NH(R^h), and -NHC(O)NH(R^h);

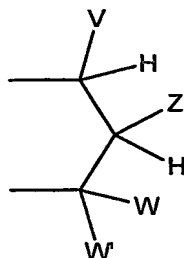
X is P(O)YR¹¹Y'R¹¹;

Y and Y' are each independently selected from the group consisting of -O-,
 15 and -NR^v-; when Y and Y' are -O-, R¹¹ attached to -O- is independently selected from the group consisting of -H, alkyl, optionally substituted aryl, optionally substituted heterocycloalkyl, optionally substituted CH₂-heterocycloalkyl wherein the cyclic moiety contains a carbonate or thiocarbonate, optionally substituted -alkylaryl, -C(R^z)₂OC(O)NR^z, -NR^z-C(O)-R^y, -C(R^z)₂-OC(O)R^y,
 20 -C(R^z)₂-O-C(O)OR^y, -C(R^z)₂OC(O)SR^y, -alkyl-S-C(O)R^y, -alkyl-S-S-alkylhydroxy, and -alkyl-S-S-S-alkylhydroxy;

when Y and Y' are -NR^v-, then R¹¹ attached to -NR^v- is independently selected from the group consisting of -H, -[C(R^z)₂]_q-COOR^y, -C(R^x)₂COOR^y, -[C(R^z)₂]_q-C(O)SR^y,
 25 and -cycloalkylene-COOR^y;

when Y is -O- and Y' is NR^v, then R¹¹ attached to -O- is independently selected from the group consisting of -H, alkyl, optionally substituted aryl, optionally substituted heterocycloalkyl, optionally substituted CH₂-heterocycloalkyl wherein the cyclic moiety contains a carbonate or thiocarbonate, optionally substituted -alkylaryl,
 30 -C(R^z)₂OC(O)NR^z, -NR^z-C(O)-R^y, -C(R^z)₂-OC(O)R^y, -C(R^z)₂-O-C(O)OR^y, -C(R^z)₂OC(O)SR^y, -alkyl-S-C(O)R^y, -alkyl-S-S-alkylhydroxy, and -alkyl-S-S-S-alkylhydroxy; and R¹¹ attached to -NR^v- is independently selected from the group consisting of -H, -[C(R^z)₂]_q-COOR^y, -C(R^x)₂COOR^y, -[C(R^z)₂]_q-C(O)SR^y, and -cycloalkylene-COOR^y;

or when Y and Y' are independently selected from -O- and -NR^v-, then together R¹¹ and R¹¹ are -alkyl-S-S-alkyl- to form a cyclic group, or together R¹¹ and R¹¹ are the group:



5 wherein:

V, W, and W' are independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted aralkyl, heterocycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, optionally substituted 1-alkenyl, and optionally substituted 1-alkynyl;

10 or together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 atoms, wherein 0-1 atoms are heteroatoms and the remaining atoms are carbon, substituted with hydroxy, acyloxy, alkylthiocarbonyloxy, alkoxy carbonyloxy, or aryloxy carbonyloxy attached to a carbon atom that is three atoms from both Y groups attached to the phosphorus; or

15 or together V and Z are connected via an additional 3-5 atoms to form a cyclic group, wherein 0-1 atoms are heteroatoms and the remaining atoms are carbon, that is fused to an aryl group at the beta and gamma position to the Y attached to the phosphorus;

20 or together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxy carbonyloxy, alkylthiocarbonyloxy, and aryloxy carbonyloxy, attached to one of said carbon atoms that is three atoms from a Y attached to the phosphorus;

25 or together Z and W are connected via an additional 3-5 atoms to form a cyclic group, wherein 0-1 atoms are heteroatoms and the remaining atoms are carbon, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

or together W and W' are connected via an additional 2-5 atoms to form a cyclic group, wherein 0-2 atoms are heteroatoms and the remaining atoms are carbon, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

Z is selected from the group consisting of -CHR^zOH, -CHR^zOC(O)R^y,
 5 -CHR^zOC(S)R^y, -CHR^zOC(S)OR^y, -CHR^zOC(O)SR^y, -CHR^zOCO₂R^y, -OR^z,
 -SR^z, -CHR^zN₃, -CH₂aryl, -CH(aryl)OH, -CH(CH=CR^z)OH, -CH(C≡CR^z)OH,
 -R^z, -NR^z, -OCOR^y, -OCO₂R^y, -SCOR^y, -SCO₂R^y, -NHCOR^z, -NHCO₂R^y, -CH₂NHaryl,
 -(CH₂)_q-OR^z, and -(CH₂)_q-SR^z;

q is an integer 2 or 3;

10 Each R^z is selected from the group consisting of R^y and -H;

Each R^y is selected from the group consisting of alkyl, aryl, heterocycloalkyl, and aralkyl;

Each R^x is independently selected from the group consisting of -H, and alkyl, or together R^x and R^x form a cyclic alkyl group;

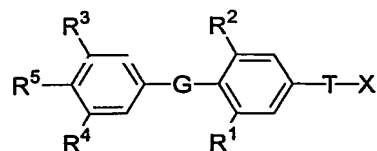
15 Each R^v is selected from the group consisting of -H, lower alkyl, acyloxyalkyl, alkoxy-carbonyloxyalkyl, and lower acyl;

with the provisos that:

- a) when G is -O-, T is -CH₂-, R¹ and R² are each bromo, R³ is *iso*-propyl, R⁴ is hydrogen, and R⁵ is -OH, then X is not P(O)(OH)₂ or P(O)(OCH₂CH₃)₂;
 20 b) V, Z, W, W' are not all -H; and
 c) when Z is -R^z, then at least one of V, W, and W' is not -H, alkyl, aralkyl, or heterocycloalkyl;

and pharmaceutically acceptable salts and prodrugs thereof and pharmaceutically acceptable salts of said prodrugs.

25 104. The method of claim 100 wherein said phosphonic acid-containing compound is a compound of Formula I:



wherein:

G is selected from the group consisting of -O-, -S-, -S(=O)-, -S(=O)₂-,
 30 -CH₂-, -CF₂-, -CHF-, -C(O)-, -CH(OH)-, -NH-, and -N(C₁-C₄ alkyl)-;

- T is selected from the group consisting of $-(CR^a_2)_k-$, $-CR^b=CR^b-(CR^a_2)_n-$, $-(CR^a_2)_n-CR^b=CR^b-$, $-(CR^a_2)-CR^b=CR^b-(CR^a_2)-$, $-O(CR^b_2)(CR^a_2)_n-$, $-S(CR^b_2)(CR^a_2)_n-$, $-N(R^c)(CR^b_2)(CR^a_2)_n-$, $-N(R^b)C(O)(CR^a_2)_n-$, $-(CR^a_2)_nCH(NR^bR^c)-$, $-C(O)(CR^a_2)_m-$, $-(CR^a_2)_mC(O)-$, $-(CR^a_2)C(O)(CR^a_2)_n-$, $-(CR^a_2)_nC(O)(CR^a_2)-$, and $-C(O)NH(CR^b_2)(CR^a_2)_p-$;
- 5 k is an integer from 0-4;
 m is an integer from 0-3;
 n is an integer from 0-2;
 p is an integer from 0-1;
- 10 Each R^a is independently selected from the group consisting of hydrogen, optionally substituted $-C_1-C_4$ alkyl, halogen, $-OH$, optionally substituted $-O-C_1-C_4$ alkyl, $-OCF_3$, optionally substituted $-S-C_1-C_4$ alkyl, $-NR^bR^c$, optionally substituted $-C_2-C_4$ alkenyl, and optionally substituted $-C_2-C_4$ alkynyl; with the proviso that when one R^a is attached to C through an O, S, or N atom, then the other R^a attached
- 15 to the same C is a hydrogen, or attached via a carbon atom;
- Each R^b is independently selected from the group consisting of hydrogen and optionally substituted $-C_1-C_4$ alkyl;
- Each R^c is independently selected from the group consisting of hydrogen, optionally substituted $-C_1-C_4$ alkyl, optionally substituted $-C(O)-C_1-C_4$ alkyl,
- 20 and $-C(O)H$;
- R^1 and R^2 are each independently selected from the group consisting of halogen, optionally substituted $-C_1-C_4$ alkyl, optionally substituted $-S-C_1-C_3$ alkyl, optionally substituted $-C_2-C_4$ alkenyl, optionally substituted $-C_2-C_4$ alkynyl, $-CF_3$, $-OCF_3$, optionally substituted $-O-C_1-C_3$ alkyl, and cyano;
- 25 R^3 and R^4 are each independently selected from the group consisting of hydrogen, halogen, $-CF_3$, $-OCF_3$, cyano, optionally substituted $-C_1-C_{12}$ alkyl, optionally substituted $-C_2-C_{12}$ alkenyl, optionally substituted $-C_2-C_{12}$ alkynyl, optionally substituted $-(CR^a_2)_m$ aryl, optionally substituted $-(CR^a_2)_m$ cycloalkyl, optionally substituted $(CR^a_2)_m$ heterocycloalkyl, $-OR^d$, $-SR^d$, $-S(=O)R^e$, $-S(=O)_2R^e$, $-S(=O)_2NR^fR^g$, $-C(O)NR^fR^g$,
- 30 $-C(O)OR^h$, $-C(O)R^e$, $-N(R^b)C(O)R^e$, $-N(R^b)C(O)NR^fR^g$, $-N(R^b)S(=O)_2R^e$, $-N(R^b)S(=O)_2NR^fR^g$, and $-NR^fR^g$;
- Each R^d is selected from the group consisting of optionally substituted $-C_1-C_{12}$ alkyl, optionally substituted $-C_2-C_{12}$ alkenyl, optionally substituted $-C_2-C_{12}$ alkynyl,

optionally substituted $-(CR^b_2)_n$ aryl, optionally substituted $-(CR^b_2)_n$ cycloalkyl, optionally substituted $-(CR^b_2)_n$ heterocycloalkyl, and $-C(O)NR^fR^g$;

Each R^e is optionally substituted $-C_1-C_{12}$ alkyl, optionally substituted $-C_2-C_{12}$ alkenyl, optionally substituted $-C_2-C_{12}$ alkynyl, optionally substituted $-(CR^a_2)_n$ aryl,
 5 optionally substituted $-(CR^a_2)_n$ cycloalkyl, and optionally substituted $-(CR^a_2)_n$ heterocycloalkyl;

R^f and R^g are each independently selected from the group consisting of hydrogen, optionally substituted $-C_1-C_{12}$ alkyl, optionally substituted $-C_2-C_{12}$ alkenyl, optionally substituted $-C_2-C_{12}$ alkynyl, optionally substituted $-(CR^b_2)_n$ aryl, optionally substituted $-(CR^b_2)_n$ cycloalkyl, and optionally substituted $-(CR^b_2)_n$ heterocycloalkyl, or R^f
 10 and R^g may together form an optionally substituted heterocyclic ring, which may contain a second heterogroup selected from the group of O, NR^c , and S, wherein said optionally substituted heterocyclic ring may be substituted with 0-4 substituents selected from the group consisting of optionally substituted $-C_1-C_4$ alkyl, $-OR^b$, oxo, cyano, $-CF_3$,
 15 optionally substituted phenyl, and $-C(O)OR^h$;

Each R^h is selected from the group consisting of optionally substituted $-C_1-C_{12}$ alkyl, optionally substituted $-C_2-C_{12}$ alkenyl, optionally substituted $-C_2-C_{12}$ alkynyl, optionally substituted $-(CR^b_2)_n$ aryl, optionally substituted $-(CR^b_2)_n$ cycloalkyl, and optionally substituted $-(CR^b_2)_n$ heterocycloalkyl;

20 R^5 is selected from the group consisting of $-OH$, optionally substituted $-OC_1-C_6$ alkyl, $-OC(O)R^e$, $-OC(O)OR^h$, $-F$, $-NHC(O)R^e$, $-NHS(=O)_2R^e$, $-NHS(=O)R^e$, $-NHC(=S)NH(R^h)$, and $-NHC(O)NH(R^h)$;

X is $P(O)YR^{11}Y'R^{11}$;

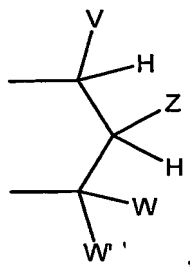
Y and Y' are each independently selected from the group consisting of $-O-$,
 25 and $-NR^v-$; when Y and Y' are $-O-$, R^{11} attached to $-O-$ is independently selected from the group consisting of $-H$, alkyl, optionally substituted aryl, optionally substituted heterocycloalkyl, optionally substituted CH_2 -heterocycloalkyl wherein the cyclic moiety contains a carbonate or thiocarbonate, optionally substituted $-alkylaryl$,
 $-C(R^z)_2OC(O)NR^z_2$, $-NR^z-C(O)-R^y$, $-C(R^z)_2-OC(O)R^y$, $-C(R^z)_2-O-C(O)OR^y$,
 30 $-C(R^z)_2OC(O)SR^y$, $-alkyl-S-C(O)R^y$, $-alkyl-S-S-alkylhydroxy$,
 and $-alkyl-S-S-S-alkylhydroxy$;

when Y and Y' are $-NR^v-$, then R^{11} attached to $-NR^v-$ is independently selected from the group consisting

of -H, $-\text{[C(R}^Z)_2\text{]}_q\text{-COOR}^Y$, $-\text{C(R}^X)_2\text{COOR}^Y$, $-\text{[C(R}^Z)_2\text{]}_q\text{-C(O)SR}^Y$,
and -cycloalkylene-COOR^Y;

when Y is -O- and Y' is NR^V, then R¹¹ attached to -O- is independently selected
from the group consisting of -H, alkyl, optionally substituted aryl, optionally substituted
5 heterocycloalkyl, optionally substituted CH₂-heterocycloalkyl wherein the cyclic moiety
contains a carbonate or thiocarbonate, optionally substituted -alkylaryl,
 $-\text{C(R}^Z)_2\text{OC(O)NR}^Z_2$, $-\text{NR}^Z\text{-C(O)-R}^Y$, $-\text{C(R}^Z)_2\text{-OC(O)R}^Y$,
 $-\text{C(R}^Z)_2\text{-O-C(O)OR}^Y$, $-\text{C(R}^Z)_2\text{OC(O)SR}^Y$, -alkyl-S-C(O)R^Y, -alkyl-S-S-alkylhydroxy,
and -alkyl-S-S-S-alkylhydroxy; and R¹¹ attached to -NR^V- is independently selected from
10 the group consisting of -H, $-\text{[C(R}^Z)_2\text{]}_q\text{-COOR}^Y$, $-\text{C(R}^X)_2\text{COOR}^Y$, $-\text{[C(R}^Z)_2\text{]}_q\text{-C(O)SR}^Y$,
and -cycloalkylene-COOR^Y;

or when Y and Y' are independently selected from -O- and -NR^V-, then together
R¹¹ and R¹¹ are -alkyl-S-S-alkyl- to form a cyclic group, or together R¹¹ and R¹¹ are the
group:



wherein:

V, W, and W' are independently selected from the group consisting of hydrogen,
optionally substituted alkyl, optionally substituted aralkyl, heterocycloalkyl, aryl,
substituted aryl, heteroaryl, substituted heteroaryl, optionally substituted 1-alkenyl, and
20 optionally substituted 1-alkynyl;

or together V and Z are connected via an additional 3-5 atoms to form a cyclic
group containing 5-7 atoms, wherein 0 – 1 atoms are heteroatoms and the remaining
atoms are carbon, substituted with hydroxy, acyloxy, alkylthiocarbonyloxy,
alkoxycarbonyloxy, or aryloxy carbonyloxy attached to a carbon atom that is three atoms
25 from both Y groups attached to the phosphorus; or

or together V and Z are connected via an additional 3-5 atoms to form a cyclic
group, wherein 0–1 atoms are heteroatoms and the remaining atoms are carbon, that is

fused to an aryl group at the beta and gamma position to the Y attached to the phosphorus;

or together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one
 5 substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to one of said carbon atoms that is three atoms from a Y attached to the phosphorus;

or together Z and W are connected via an additional 3-5 atoms to form a cyclic group, wherein 0-1 atoms are heteroatoms and the remaining atoms are carbon, and V
 10 must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

or together W and W' are connected via an additional 2-5 atoms to form a cyclic group, wherein 0-2 atoms are heteroatoms and the remaining atoms are carbon, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

Z is selected from the group consisting of $-\text{CHR}^z\text{OH}$, $-\text{CHR}^z\text{OC}(\text{O})\text{R}^y$,
 15 $-\text{CHR}^z\text{OC}(\text{S})\text{R}^y$, $-\text{CHR}^z\text{OC}(\text{S})\text{OR}^y$, $-\text{CHR}^z\text{OC}(\text{O})\text{SR}^y$, $-\text{CHR}^z\text{OCO}_2\text{R}^y$, $-\text{OR}^z$, $-\text{SR}^z$, $-\text{CHR}^z\text{N}_3$, $-\text{CH}_2\text{aryl}$, $-\text{CH}(\text{aryl})\text{OH}$, $-\text{CH}(\text{CH}=\text{CR}^z_2)\text{OH}$, $-\text{CH}(\text{C}\equiv\text{CR}^z_2)\text{OH}$, $-\text{R}^z$, $-\text{NR}^z_2$, $-\text{OCOR}^y$, $-\text{OCO}_2\text{R}^y$, $-\text{SCOR}^y$, $-\text{SCO}_2\text{R}^y$, $-\text{NHCOR}^z$, $-\text{NHCO}_2\text{R}^y$, $-\text{CH}_2\text{NHaryl}$, $-(\text{CH}_2)_q-\text{OR}^z$, and $-(\text{CH}_2)_q-\text{SR}^z$;

q is an integer 2 or 3;

20 Each R^z is selected from the group consisting of R^y and $-\text{H}$;

Each R^y is selected from the group consisting of alkyl, aryl, heterocycloalkyl, and aralkyl;

Each R^x is independently selected from the group consisting of $-\text{H}$, and alkyl, or together R^x and R^x form a cyclic alkyl group;

25 Each R^y is selected from the group consisting of $-\text{H}$, lower alkyl, acyloxyalkyl, alkoxycarbonyloxyalkyl, and lower acyl;

with the provisos that:

a) when G is $-\text{O}-$, T is $-(\text{CH}_2)_{0-4}-$, R^1 and R^2 are independently halogen, alkyl of 1 to 3 carbons, and cycloalkyl of 3 to 5 carbons, R^3 is alkyl of 1 to 4 carbons or
 30 cycloalkyl of 3 to 7 carbons, R^4 is hydrogen, and R^5 is $-\text{OH}$, then X is not $-\text{P}(\text{O})(\text{OH})_2$ or $-\text{P}(\text{O})(\text{O-lower alkyl})_2$;

b) when G is $-\text{O}-$, R^5 is $-\text{NHC}(\text{O})\text{R}^e$, $-\text{NHS}(=\text{O})_{1-2}\text{R}^e$, $-\text{NHC}(\text{S})\text{NH}(\text{R}^h)$, or $-\text{NHC}(\text{O})\text{NH}(\text{R}^h)$, T is $-(\text{CH}_2)_m-$, $-\text{CH}=\text{CH}-$, $-\text{O}(\text{CH}_2)_{1-2}-$, or $-\text{NH}(\text{CH}_2)_{1-2}-$, then X is not $-\text{P}(\text{O})(\text{OH})_2$ or $-\text{P}(\text{O})(\text{OH})\text{NH}_2$;

c) V, Z, W, W' are not all -H; and

d) when Z is $-R^z$, then at least one of V, W, and W' is not -H, alkyl, aralkyl, or heterocycloalkyl;

and pharmaceutically acceptable salts and prodrugs thereof and pharmaceutically acceptable salts of said prodrugs.

105. The method of claim 103 wherein when G is -O-, T is $-\text{CH}_2-$, R^1 and R^2 are each bromo, R^3 is *iso*-propyl, and R^5 is -OH, then R^4 is not hydrogen.

106. The method of claim 104 wherein when G is -O-, T is $-(\text{CH}_2)_0-$, R^1 and R^2 are independently selected from the group consisting of halogen, alkyl of 1 to 3 carbons, and cycloalkyl of 3 to 5 carbons, R^3 is alkyl of 1 to 4 carbons or cycloalkyl of 3 to 7 carbons, and R^5 is -OH, then R^4 is not hydrogen; and wherein when G is -O-, R^5 is selected from the group consisting of $\text{NHC}(\text{O})\text{R}^e$, $-\text{NHS}(=\text{O})_{1-2}\text{R}^e$, $-\text{NHC}(=\text{S})\text{NH}(\text{R}^h)$, and $-\text{NHC}(\text{O})\text{NH}(\text{R}^h)$, T is selected from the group consisting of $-(\text{CH}_2)_m-$, $-\text{CH}=\text{CH}-$, $-\text{O}(\text{CH}_2)_{1-2}-$, and $-\text{NH}(\text{CH}_2)_{1-2}-$, then R^4 is not hydrogen.

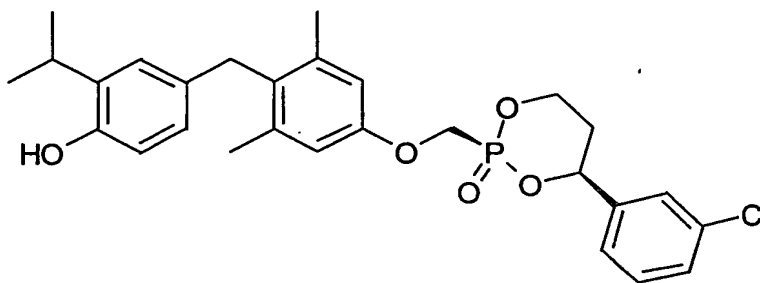
107. The method of claim 83 wherein said metabolic disease is NASH.

108. The method of claim 83 wherein said metabolic disease is selected from the group consisting of impaired glucose tolerance, diabetes, and metabolic syndromex.

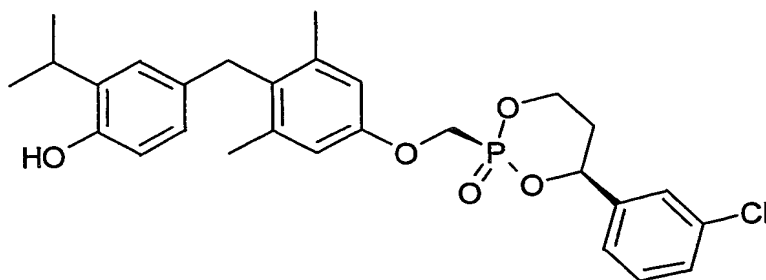
109. The method of claim 96 wherein said metabolic disease is hypercholesterolemia.

110. The method of claim 96 wherein said metabolic disease is obesity.

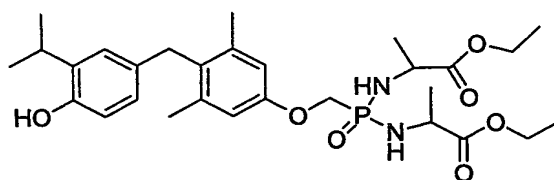
111. The method of claim 109 wherein said compound of Formula I is:



112. The method of claim 110 wherein said compound of Formula I is:

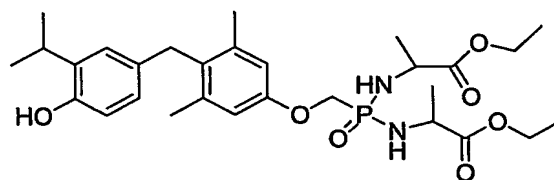


113. The method of claim 109 wherein said compound of Formula I is:

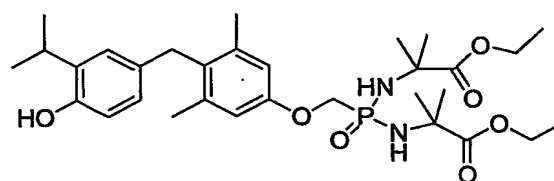


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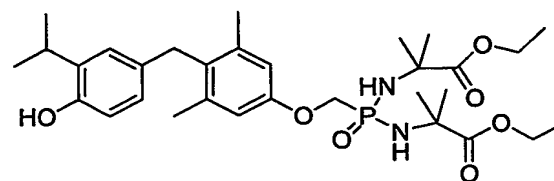
114. The method of claim 110 wherein said compound of Formula I is:



115. The method of claim 109 wherein said compound of Formula I is:

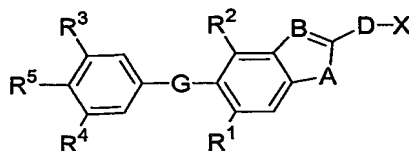


116. The method of claim 110 wherein said compound of Formula I is:



10

117. A compound of Formula II:



wherein:

A is selected from the group consisting of -NRⁱ-, -O-, and -S-;

5 B is selected from the group consisting of -CR^b-, and -N-;

Rⁱ is selected from the group consisting of hydrogen, -C(O)C₁-C₄ alkyl, -C₁-C₄ alkyl, and -C₁-C₄-aryl;

R^b is selected from the group consisting of hydrogen and optionally substituted -C₁-C₄ alkyl;

10 G is selected from the group consisting of -O-, -S-, -S(=O)-, -S(=O)₂-, -CH₂-, -CF₂-, -CHF-, -C(O)-, -CH(OH)-, -NH-, and -N(C₁-C₄ alkyl)-;

D is selected from the group consisting of a bond, -(CR^a)₂-, and -C(O)-;

Each R^a is independently selected from the group consisting of hydrogen, optionally substituted -C₁-C₄ alkyl, halogen, -OH, optionally substituted -O-C₁-C₄ alkyl, -OCF₃, optionally substituted -S-C₁-C₄ alkyl, -NR^bR^c, optionally substituted -C₂-C₄ alkenyl, and optionally substituted -C₂-C₄ alkynyl; with the proviso that when one R^a is attached to C through an O, S, or N atom, then the other R^a attached to the same C is a hydrogen, or attached via a carbon atom;

20 R¹ and R² are each independently selected from the group consisting of halogen, optionally substituted -C₁-C₄ alkyl, optionally substituted -S-C₁-C₃ alkyl, optionally substituted -C₂-C₄ alkenyl, optionally substituted -C₂-C₄ alkynyl, -CF₃, -OCF₃, optionally substituted -O-C₁-C₃ alkyl, and cyano;

25 R³ and R⁴ are each independently selected from the group consisting of hydrogen, halogen, -CF₃, -OCF₃, cyano, optionally substituted -C₁-C₁₂ alkyl, optionally substituted -C₂-C₁₂ alkenyl, optionally substituted -C₂-C₁₂ alkynyl, optionally substituted -(CR^a)_maryl, optionally substituted -(CR^a)_mcycloalkyl, optionally substituted -(CR^a)_mheterocycloalkyl, -OR^d, -SR^d, -S(=O)R^e, -S(=O)₂R^e, -S(=O)₂NR^fR^g, -C(O)NR^fR^g, -C(O)OR^h, -C(O)R^e, -N(R^b)C(O)R^e, -N(R^b)C(O)NR^fR^g, -N(R^b)S(=O)₂R^e, -N(R^b)S(=O)₂NR^fR^g, and -NR^fR^g;

Each R^d is selected from the group consisting of optionally substituted $-C_1-C_{12}$ alkyl, optionally substituted $-C_2-C_{12}$ alkenyl, optionally substituted $-C_2-C_{12}$ alkynyl, optionally substituted $-(CR^b_2)_n$ aryl, optionally substituted $-(CR^b_2)_n$ cycloalkyl, optionally substituted $-(CR^b_2)_n$ heterocycloalkyl, and $-C(O)NR^fR^g$;

- 5 Each R^e is selected from the group consisting of optionally substituted $-C_1-C_{12}$ alkyl, optionally substituted $-C_2-C_{12}$ alkenyl, optionally substituted $-C_2-C_{12}$ alkynyl, optionally substituted $-(CR^a_2)_n$ aryl, optionally substituted $-(CR^a_2)_n$ cycloalkyl, and optionally substituted $-(CR^a_2)_n$ heterocycloalkyl;

- R^f and R^g are each independently selected from the group consisting of hydrogen, 10 optionally substituted $-C_1-C_{12}$ alkyl, optionally substituted $-C_2-C_{12}$ alkenyl, optionally substituted $-C_2-C_{12}$ alkynyl, optionally substituted $-(CR^b_2)_n$ aryl, optionally substituted $-(CR^b_2)_n$ cycloalkyl, and optionally substituted $-(CR^b_2)_n$ heterocycloalkyl, or R^f and R^g may together form an optionally substituted heterocyclic ring, which may contain a second heterogroup selected from the group consisting of O, NR^e , and S, wherein said 15 optionally substituted heterocyclic ring may be substituted with 0-4 substituents selected from the group consisting of optionally substituted $-C_1-C_4$ alkyl, $-OR^b$, oxo, cyano, $-CF_3$, optionally substituted phenyl, and $-C(O)OR^h$;

- Each R^h is selected from the group consisting of optionally substituted $-C_1-C_{12}$ alkyl, optionally substituted $-C_2-C_{12}$ alkenyl, optionally substituted $-C_2-C_{12}$ alkynyl, 20 optionally substituted $-(CR^b_2)_n$ aryl, optionally substituted $-(CR^b_2)_n$ cycloalkyl, and optionally substituted $-(CR^b_2)_n$ heterocycloalkyl;

R^5 is selected from the group consisting of $-OH$, optionally substituted $-OC_1-C_6$ alkyl, $-OC(O)R^e$, $-OC(O)OR^h$, $-F$, $-NHC(O)R^e$, $-NHS(=O)R^e$, $-NHS(=O)_2R^e$, $-NHC(=S)NH(R^h)$, and $-NHC(O)NH(R^h)$;

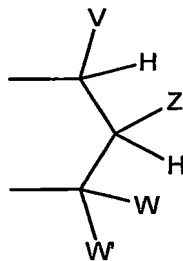
- 25 X is $P(O)YR^{11}Y'R^{11}$;

- Y and Y' are each independently selected from the group consisting of $-O-$, and $-NR^v-$; when Y and Y' are $-O-$, R^{11} attached to $-O-$ is independently selected from the group consisting of $-H$, alkyl, optionally substituted aryl, optionally substituted heterocycloalkyl, optionally substituted CH_2 -heterocycloalkyl wherein the cyclic moiety 30 contains a carbonate or thiocarbonate, optionally substituted $-alkylaryl$, $-C(R^z)_2OC(O)NR^z_2$, $-NR^z-C(O)-R^y$, $-C(R^z)_2-OC(O)R^y$, $-C(R^z)_2-O-C(O)OR^y$, $-C(R^z)_2OC(O)SR^y$, $-alkyl-S-C(O)R^y$, $-alkyl-S-S-alkylhydroxy$, and $-alkyl-S-S-S-alkylhydroxy$;

when Y and Y' are $-NR^v$ -, then R^{11} attached to $-NR^v$ - is independently selected from the group consisting of $-H$ -, $-[C(R^z)_2]_q-COOR^y$ -, $-C(R^x)_2COOR^y$ -, $-[C(R^z)_2]_q-C(O)SR^y$ -, and $-cycloalkylene-COOR^y$;

- 5 when Y is $-O-$ and Y' is NR^v -, then R^{11} attached to $-O-$ is independently selected from the group consisting of $-H$ -, alkyl-, optionally substituted aryl-, optionally substituted heterocycloalkyl-, optionally substituted CH_2 -heterocycloalkyl wherein the cyclic moiety contains a carbonate or thiocarbonate, optionally substituted $-alkylaryl$ -, $-C(R^z)_2OC(O)NR^z_2$ -, $-NR^z-C(O)-R^y$ -, $-C(R^z)_2-OC(O)R^y$ -, $-C(R^z)_2-O-C(O)OR^y$ -, $-C(R^z)_2OC(O)SR^y$ -, $-alkyl-S-C(O)R^y$ -, $-alkyl-S-S-alkylhydroxy$ -, and $-alkyl-S-S-S-alkylhydroxy$; and R^{11} attached to $-NR^v$ - is independently selected from the group consisting of $-H$ -, $-[C(R^z)_2]_q-COOR^y$ -, $-C(R^x)_2COOR^y$ -, $-[C(R^z)_2]_q-C(O)SR^y$ -, and $-cycloalkylene-COOR^y$;
- 10

- or when Y and Y' are independently selected from $-O-$ and $-NR^v$ -, then together R^{11} and R^{11} are $-alkyl-S-S-alkyl-$ to form a cyclic group, or together R^{11} and R^{11} are the group:
- 15



wherein:

- V, W, and W' are independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted aralkyl, heterocycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, optionally substituted 1-alkenyl, and optionally substituted 1-alkynyl;
- 20

- or together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 atoms, wherein 0-1 atoms are heteroatoms and the remaining atoms are carbon, substituted with hydroxy, acyloxy, alkylthiocarbonyloxy, alkoxy carbonyloxy, or aryloxy carbonyloxy attached to a carbon atom that is three atoms from both Y groups attached to the phosphorus; or
- 25

or together V and Z are connected via an additional 3-5 atoms to form a cyclic group, wherein 0-1 atoms are heteroatoms and the remaining atoms are carbon, that is fused to an aryl group at the beta and gamma position to the Y attached to the phosphorus;

5 or together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to one of said carbon atoms that is three atoms from a Y attached to the phosphorus;

10 or together Z and W are connected via an additional 3-5 atoms to form a cyclic group, wherein 0-1 atoms are heteroatoms and the remaining atoms are carbon, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

or together W and W' are connected via an additional 2-5 atoms to form a cyclic group, wherein 0-2 atoms are heteroatoms and the remaining atoms are carbon, and V
15 must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

Z is selected from the group consisting of $-\text{CHR}^z\text{OH}$, $-\text{CHR}^z\text{OC}(\text{O})\text{R}^y$, $-\text{CHR}^z\text{OC}(\text{S})\text{R}^y$, $-\text{CHR}^z\text{OC}(\text{S})\text{OR}^y$, $-\text{CHR}^z\text{OC}(\text{O})\text{SR}^y$, $-\text{CHR}^z\text{OCO}_2\text{R}^y$, $-\text{OR}^z$, $-\text{SR}^z$, $-\text{CHR}^z\text{N}_3$, $-\text{CH}_2\text{aryl}$, $-\text{CH}(\text{aryl})\text{OH}$, $-\text{CH}(\text{CH}=\text{CR}^z_2)\text{OH}$, $-\text{CH}(\text{C}\equiv\text{CR}^z)\text{OH}$, $-\text{R}^z$, $-\text{NR}^z_2$, $-\text{OCOR}^y$, $-\text{OCO}_2\text{R}^y$, $-\text{SCOR}^y$, $-\text{SCO}_2\text{R}^y$, $-\text{NHCOR}^z$, $-\text{NHCO}_2\text{R}^y$, $-\text{CH}_2\text{NHaryl}$,
20 $-(\text{CH}_2)_q-\text{OR}^z$, and $-(\text{CH}_2)_q-\text{SR}^z$;

q is an integer 2 or 3;

Each R^z is selected from the group consisting of R^y and $-\text{H}$;

Each R^y is selected from the group consisting of alkyl, aryl, heterocycloalkyl, and aralkyl;

25 Each R^x is independently selected from the group consisting of $-\text{H}$, and alkyl, or together R^x and R^x form a cyclic alkyl group;

Each R^v is selected from the group consisting of $-\text{H}$, lower alkyl, acyloxyalkyl, alkoxycarbonyloxyalkyl, and lower acyl;

with the provisos that:

30 a) V, Z, W, W' are not all $-\text{H}$; and
b) when Z is $-\text{R}^z$, then at least one of V, W, and W' is not $-\text{H}$, alkyl, aralkyl, or heterocycloalkyl;

and pharmaceutically acceptable salts and prodrugs thereof and pharmaceutically acceptable salts of said prodrugs.

118. The compound of claim 117 wherein G is selected from the group consisting of -O- and -CH₂-.
119. The compound of claim 117 wherein D is selected from the group consisting of a bond and -CH₂-.
- 5 120. The compound of claim 117 wherein A is selected from the group consisting of -NH-, -NMe-, -O-, and -S-.
121. The compound of claim 117 wherein B is selected from the group consisting of -CH₂-, CMe-, and -N-.
122. The compound of claim 117 wherein R¹ and R² are the same and are
10 selected from the group consisting of halogen, -C₁-C₄ alkyl, -CF₃, and cyano.
123. The compound of claim 117 wherein R¹ and R² are different and are selected from the group consisting of halogen, -C₁-C₄ alkyl, -CF₃, and cyano.
124. The compound of claim 117 wherein R⁴ is selected from the group consisting of hydrogen, halogen, -C₁-C₄ alkyl, cyano and CF₃.
- 15 125. The compound of claim 117 wherein R⁵ is selected from the group consisting of -OH, -OC(O)R^e, -OC(O)OR^h, -F, and -NHC(O)R^e.
126. The compound of claim 117 wherein R³ is selected from the group consisting of halogen, optionally substituted -C₁-C₆ alkyl, -CF₃, cyano, -C(O)NR^fR^g, optionally substituted -(CR^a)_naryl, -SO₂NR^fR^g, and -SO₂R^e.
- 20 127. The compound of claim 117 wherein X is selected from the group consisting of -PO₃H₂, -P(O)[-OCR^zOC(O)R^y]₂, -P(O)[-OCR^zOC(O)OR^y]₂, -P(O)[-N(H)CR^zC(O)OR^y]₂, -P(O)[-N(H)CR^zC(O)OR^y][OR¹¹], and -P(O)[-OCH(V)CH₂CH₂O-], wherein V is selected from the group consisting of optionally substituted aryl, aryl, heteroaryl, and optionally substituted heteroaryl.
- 25 128. The compound of claim 117 wherein G is selected from the group consisting of -O- and -CH₂-; D is selected from the group consisting of a bond and -CH₂-; A is selected from the group consisting of -NH-, -NMe-, -O-, and -S-; B is selected from the group consisting of -CH-, -CMe-, and -N-; R¹ and R² are each independently selected from the group consisting of halogen, -C₁-C₄ alkyl, -CF₃, and cyano; R⁴ is
30 selected from the group consisting of hydrogen, halogen, -C₁-C₄ alkyl, cyano and CF₃; R⁵ is selected from the group consisting of -OH, -OC(O)R^e, -OC(O)OR^h, -F, and -NHC(O)R^e; R³ is selected from the group consisting of halogen, optionally substituted -C₁-C₆ alkyl, -CF₃, cyano, -C(O)NR^fR^g, optionally substituted -(CR^a)_naryl, -SO₂NR^fR^g, and -SO₂R^e; and X is selected from the group

consisting of $-\text{PO}_3\text{H}_2$, $-\text{P}(\text{O})[-\text{OCR}^z\text{OC}(\text{O})\text{R}^y]_2$,
 $-\text{P}(\text{O})[-\text{OCR}^z\text{OC}(\text{O})\text{OR}^y]_2$, $-\text{P}(\text{O})[-\text{N}(\text{H})\text{CR}^z\text{C}(\text{O})\text{OR}^y]_2$,
 $-\text{P}(\text{O})[-\text{N}(\text{H})\text{CR}^z\text{C}(\text{O})\text{OR}^y][-\text{OR}^{11}]$ and $-\text{P}(\text{O})[-\text{OCH}(\text{V})\text{CH}_2\text{CH}_2\text{O}-]$, wherein V is
 5 optionally substituted heteroaryl.

129. The compound of claim 128 wherein G is selected from the group
 consisting of $-\text{O}-$ and $-\text{CH}_2-$; D is selected from the group consisting of a bond and $-\text{CH}_2-$;
 A is selected from the group consisting of $-\text{NH}-$, $-\text{NMe}-$, $-\text{O}-$, and $-\text{S}-$; B is selected from
 the group consisting of $-\text{CH}-$, $-\text{CMe}-$ and $-\text{N}-$; R^1 and R^2 are each independently selected
 10 from the group consisting of iodo, bromo, chloro, methyl, and cyano; R^4 is selected from
 the group consisting of hydrogen and halogen; R^5 is selected from the group consisting
 of $-\text{OH}$ and $-\text{OC}(\text{O})\text{R}^e$; and R^3 is selected from the group consisting of halogen,
 optionally substituted $-\text{C}_1-\text{C}_6$ alkyl, optionally substituted $-\text{CH}_2\text{aryl}$, optionally
 substituted $-\text{CH}(\text{OH})\text{aryl}$, $-\text{C}(\text{O})$ -amido, $-\text{S}(=\text{O})_2$ -amido, wherein the amido group is
 15 selected from the group consisting of phenethylamino, piperidinyl, 4-methylpiperizinyl,
 morpholinyl, cyclohexylamino, aniliny, and indolinyl, and $-\text{SO}_2\text{R}^e$ wherein R^e is
 selected from the group consisting of phenyl, 4-chlorophenyl, 4-fluorophenyl, and
 4-pyridyl.

130. The compound of claim 129 wherein G is $-\text{O}-$; D is a bond; A is selected
 20 from the group consisting of $-\text{NH}-$ and $-\text{NMe}-$; B is selected from the group consisting of
 $-\text{CH}-$ and $-\text{CMe}-$; R^1 and R^2 are each bromo; R^4 is selected from the group consisting of
 hydrogen and iodo; R^5 is $-\text{OH}$; and R^3 is isopropyl.

131. The compound of claim 130 wherein X is selected from the group
 consisting of $-\text{PO}_3\text{H}_2$, $-\text{P}(\text{O})[-\text{OCH}_2\text{OC}(\text{O})-t\text{-butyl}]_2$, $-\text{P}(\text{O})[-\text{OCH}_2\text{OC}(\text{O})\text{O}-i\text{-propyl}]_2$,
 25 $-\text{P}(\text{O})[-\text{N}(\text{H})\text{CH}(\text{CH}_3)\text{C}(\text{O})\text{OCH}_2\text{CH}_3]_2$, $-\text{P}(\text{O})[-\text{N}(\text{H})\text{C}(\text{CH}_3)_2\text{C}(\text{O})\text{OCH}_2\text{CH}_3]_2$,
 $-\text{P}(\text{O})[-\text{N}(\text{H})\text{CH}(\text{CH}_3)\text{C}(\text{O})\text{OCH}_2\text{CH}_3][3,4\text{-methylenedioxyphenyl}]$,
 $-\text{P}(\text{O})[-\text{N}(\text{H})\text{C}(\text{CH}_3)_2\text{C}(\text{O})\text{OCH}_2\text{CH}_3][3,4\text{-methylenedioxyphenyl}]$,
 and $-\text{P}(\text{O})[-\text{OCH}(3\text{-chlorophenyl})\text{CH}_2\text{CH}_2\text{O}-]$.

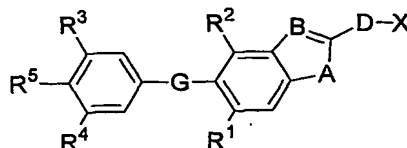
132. The compound of claim 129 wherein G is $-\text{O}-$; D is a bond; A is $-\text{O}-$; B is
 30 selected from the group consisting of $-\text{CH}-$ and $-\text{CMe}-$; R^1 and R^2 are each bromo; R^4 is
 selected from the group consisting of hydrogen and iodo; R^5 is $-\text{OH}$; and R^3 is isopropyl.

133. The compound of claim 132 wherein X is selected from the group
 consisting of $-\text{PO}_3\text{H}_2$, $-\text{P}(\text{O})[-\text{OCH}_2\text{OC}(\text{O})-t\text{-butyl}]_2$, $-\text{P}(\text{O})[-\text{OCH}_2\text{OC}(\text{O})\text{O}-i\text{-propyl}]_2$,
 $-\text{P}(\text{O})[-\text{N}(\text{H})\text{CH}(\text{CH}_3)\text{C}(\text{O})\text{OCH}_2\text{CH}_3]_2$, $-\text{P}(\text{O})[-\text{N}(\text{H})\text{C}(\text{CH}_3)_2\text{C}(\text{O})\text{OCH}_2\text{CH}_3]_2$,

-P(O)[-N(H)CH(CH₃)C(O)OCH₂CH₃][3,4-methylenedioxyphenyl],
 -P(O)[-N(H)C(CH₃)₂C(O)OCH₂CH₃][3,4-methylenedioxyphenyl],
 and -P(O)[-OCH(3-chlorophenyl)CH₂CH₂O-].

134. The compound as in any of claims 117, 128, 129, 131, and 133 wherein X
 5 is -PO₃H₂.

135. The method of claim 83 wherein said phosphonic acid-containing
 compound is a compound of Formula II:



wherein:

- 10 A is selected from the group consisting of -NRⁱ-, -O-, and -S-;
 B is selected from the group consisting of -CR^b-, and -N-;
 Rⁱ is selected from the group consisting of hydrogen, -C(O)C₁-C₄ alkyl,
 -C₁-C₄ alkyl, and -C₁-C₄-aryl;
 R^b is selected from the group consisting of hydrogen and optionally
 15 substituted -C₁-C₄ alkyl;
 G is selected from the group consisting of -O-, -S-, -S(=O)-, -S(=O)₂-,
 -CH₂-, -CF₂-, -CHF-, -C(O)-, -CH(OH)-, -NH-, and -N(C₁-C₄ alkyl)-;
 D is selected from the group consisting of a bond, -(CR^a)₂-, and -C(O)-;
 Each R^a is independently selected from the group consisting of hydrogen,
 20 optionally substituted -C₁-C₄ alkyl, halogen, -OH, optionally substituted -O-C₁-C₄
 alkyl, -OCF₃, optionally substituted -S-C₁-C₄ alkyl, -NR^bR^c, optionally
 substituted -C₂-C₄ alkenyl, and optionally substituted -C₂-C₄ alkynyl; with the proviso
 that when one R^a is attached to C through an O, S, or N atom, then the other R^a attached
 to the same C is a hydrogen, or attached via a carbon atom;
 25 R¹ and R² are each independently selected from the group consisting of halogen,
 optionally substituted -C₁-C₄ alkyl, optionally substituted -S-C₁-C₃ alkyl, optionally
 substituted -C₂-C₄ alkenyl, optionally substituted -C₂-C₄ alkynyl, -CF₃, -OCF₃, optionally
 substituted -O-C₁-C₃ alkyl, and cyano;
 R³ and R⁴ are each independently selected from the group consisting of hydrogen,
 30 halogen, -CF₃, -OCF₃, cyano, optionally substituted -C₁-C₁₂ alkyl, optionally

substituted $-C_2-C_{12}$ alkenyl, optionally substituted $-C_2-C_{12}$ alkynyl, optionally substituted $-(CR^a)_m$ aryl, optionally substituted $-(CR^a)_m$ cycloalkyl, optionally substituted $-(CR^a)_m$ heterocycloalkyl, $-OR^d$, $-SR^d$, $-S(=O)R^e$, $-S(=O)_2R^e$, $-S(=O)_2NR^fR^g$, $-C(O)NR^fR^g$, $-C(O)OR^h$, $-C(O)R^e$, $-N(R^b)C(O)R^e$, $-N(R^b)C(O)NR^fR^g$, $-N(R^b)S(=O)_2R^e$,
 5 $-N(R^b)S(=O)_2NR^fR^g$, and $-NR^fR^g$;

Each R^d is selected from the group consisting of optionally substituted $-C_1-C_{12}$ alkyl, optionally substituted $-C_2-C_{12}$ alkenyl, optionally substituted $-C_2-C_{12}$ alkynyl, optionally substituted $-(CR^b)_n$ aryl, optionally substituted $-(CR^b)_n$ cycloalkyl, optionally substituted $-(CR^b)_n$ heterocycloalkyl, and $-C(O)NR^fR^g$;

10 Each R^e is selected from the group consisting of optionally substituted $-C_1-C_{12}$ alkyl, optionally substituted $-C_2-C_{12}$ alkenyl, optionally substituted $-C_2-C_{12}$ alkynyl, optionally substituted $-(CR^a)_n$ aryl, optionally substituted $-(CR^a)_n$ cycloalkyl, and optionally substituted $-(CR^a)_n$ heterocycloalkyl;

R^f and R^g are each independently selected from the group consisting of hydrogen,
 15 optionally substituted $-C_1-C_{12}$ alkyl, optionally substituted $-C_2-C_{12}$ alkenyl, optionally substituted $-C_2-C_{12}$ alkynyl, optionally substituted $-(CR^b)_n$ aryl, optionally substituted $-(CR^b)_n$ cycloalkyl, and optionally substituted $-(CR^b)_n$ heterocycloalkyl, or R^f and R^g may together form an optionally substituted heterocyclic ring, which may contain a second heterogroup selected from the group consisting of O, NR^e , and S, wherein said
 20 optionally substituted heterocyclic ring may be substituted with 0-4 substituents selected from the group consisting of optionally substituted $-C_1-C_4$ alkyl, $-OR^b$, oxo, cyano, $-CF_3$, optionally substituted phenyl, and $-C(O)OR^h$;

Each R^h is selected from the group consisting of optionally substituted $-C_1-C_{12}$ alkyl, optionally substituted $-C_2-C_{12}$ alkenyl, optionally substituted $-C_2-C_{12}$ alkynyl,
 25 optionally substituted $-(CR^b)_n$ aryl, optionally substituted $-(CR^b)_n$ cycloalkyl, and optionally substituted $-(CR^b)_n$ heterocycloalkyl;

R^5 is selected from the group consisting of $-OH$, optionally substituted $-OC_1-C_6$ alkyl, $-OC(O)R^e$, $-OC(O)OR^h$, $-F$, $-NHC(O)R^e$, $-NHS(=O)R^e$, $-NHS(=O)_2R^e$, $-NHC(=S)NH(R^h)$, and $-NHC(O)NH(R^h)$;

30 X is $P(O)YR^{11}Y'R^{11}$;

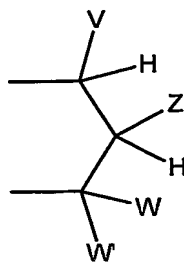
Y and Y' are each independently selected from the group consisting of $-O-$, and $-NR^v-$; when Y and Y' are $-O-$, R^{11} attached to $-O-$ is independently selected from the group consisting of $-H$, alkyl, optionally substituted aryl, optionally substituted heterocycloalkyl, optionally substituted CH_2 -heterocycloalkyl wherein the cyclic moiety

contains a carbonate or thiocarbonate, optionally substituted -alkylaryl,
 $-C(R^Z)_2OC(O)NR^Z$, $-NR^Z-C(O)-R^Y$, $-C(R^Z)_2-OC(O)R^Y$,
 $-C(R^Z)_2-O-C(O)OR^Y$, $-C(R^Z)_2OC(O)SR^Y$, -alkyl-S-C(O)R^Y, -alkyl-S-S-alkylhydroxy,
 and -alkyl-S-S-S-alkylhydroxy;

5 when Y and Y' are $-NR^V$ -, then R¹¹ attached to $-NR^V$ - is independently selected
 from the group consisting
 of -H, $-[C(R^Z)_2]_q-COOR^Y$, $-C(R^X)_2COOR^Y$, $-[C(R^Z)_2]_q-C(O)SR^Y$,
 and -cycloalkylene-COOR^Y;

 when Y is -O- and Y' is NR^V , then R¹¹ attached to -O- is independently selected
 10 from the group consisting of -H, alkyl, optionally substituted aryl, optionally substituted
 heterocycloalkyl, optionally substituted CH₂-heterocycloalkyl wherein the cyclic moiety
 contains a carbonate or thiocarbonate, optionally
 substituted -alkylaryl, $-C(R^Z)_2OC(O)NR^Z$, $-NR^Z-C(O)-R^Y$, $-C(R^Z)_2-OC(O)R^Y$,
 $-C(R^Z)_2-O-C(O)OR^Y$, $-C(R^Z)_2OC(O)SR^Y$, -alkyl-S-C(O)R^Y, -alkyl-S-S-alkylhydroxy,
 15 and -alkyl-S-S-S-alkylhydroxy; and R¹¹ attached to $-NR^V$ - is independently selected from
 the group consisting of -H, $-[C(R^Z)_2]_q-COOR^Y$, $-C(R^X)_2COOR^Y$, $-[C(R^Z)_2]_q-C(O)SR^Y$,
 and -cycloalkylene-COOR^Y;

 or when Y and Y' are independently selected from -O- and $-NR^V$ -, then together
 R¹¹ and R¹¹ are -alkyl-S-S-alkyl- to form a cyclic group, or together R¹¹ and R¹¹ are the
 20 group:



wherein:

V, W, and W' are independently selected from the group consisting of hydrogen,
 optionally substituted alkyl, optionally substituted aralkyl, heterocycloalkyl, aryl,
 25 substituted aryl, heteroaryl, substituted heteroaryl, optionally substituted 1-alkenyl, and
 optionally substituted 1-alkynyl;

 or together V and Z are connected via an additional 3-5 atoms to form a cyclic
 group containing 5-7 atoms, wherein 0-1 atoms are heteroatoms and the remaining

atoms are carbon, substituted with hydroxy, acyloxy, alkylthiocarbonyloxy, alkoxy carbonyloxy, or aryloxy carbonyloxy attached to a carbon atom that is three atoms from both Y groups attached to the phosphorus; or

or together V and Z are connected via an additional 3-5 atoms to form a cyclic group, wherein 0-1 atoms are heteroatoms and the remaining atoms are carbon, that is fused to an aryl group at the beta and gamma position to the Y attached to the phosphorus;

or together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxy carbonyloxy, alkylthiocarbonyloxy, and aryloxy carbonyloxy, attached to one of said carbon atoms that is three atoms from a Y attached to the phosphorus;

or together Z and W are connected via an additional 3-5 atoms to form a cyclic group, wherein 0-1 atoms are heteroatoms and the remaining atoms are carbon, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

or together W and W' are connected via an additional 2-5 atoms to form a cyclic group, wherein 0-2 atoms are heteroatoms and the remaining atoms are carbon, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

Z is selected from the group consisting of $-\text{CHR}^z\text{OH}$, $-\text{CHR}^z\text{OC}(\text{O})\text{R}^y$, $-\text{CHR}^z\text{OC}(\text{S})\text{R}^y$, $-\text{CHR}^z\text{OC}(\text{S})\text{OR}^y$, $-\text{CHR}^z\text{OC}(\text{O})\text{SR}^y$, $-\text{CHR}^z\text{OCO}_2\text{R}^y$, $-\text{OR}^z$, $-\text{SR}^z$, $-\text{CHR}^z\text{N}_3$, $-\text{CH}_2\text{aryl}$, $-\text{CH}(\text{aryl})\text{OH}$, $-\text{CH}(\text{CH}=\text{CR}^z_2)\text{OH}$, $-\text{CH}(\text{C}\equiv\text{CR}^z_2)\text{OH}$, $-\text{R}^z$, $-\text{NR}^z_2$, $-\text{OCOR}^y$, $-\text{OCO}_2\text{R}^y$, $-\text{SCOR}^y$, $-\text{SCO}_2\text{R}^y$, $-\text{NHCOR}^z$, $-\text{NHCO}_2\text{R}^y$, $-\text{CH}_2\text{NHaryl}$, $-(\text{CH}_2)_q-\text{OR}^z$, and $-(\text{CH}_2)_q-\text{SR}^z$;

q is an integer 2 or 3;

Each R^z is selected from the group consisting of R^y and $-\text{H}$;

Each R^y is selected from the group consisting of alkyl, aryl, heterocycloalkyl, and aralkyl;

Each R^x is independently selected from the group consisting of $-\text{H}$, and alkyl, or together R^x and R^x form a cyclic alkyl group;

Each R^v is selected from the group consisting of $-\text{H}$, lower alkyl, acyloxyalkyl, alkoxy carbonyloxyalkyl, and lower acyl;

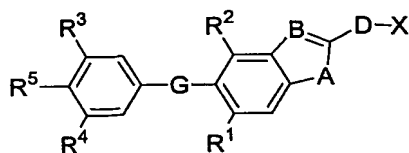
with the provisos that:

a) V, Z, W, W' are not all $-\text{H}$; and

b) when Z is $-R^Z$, then at least one of V, W, and W' is not -H, alkyl, aralkyl, or heterocycloalkyl;

and pharmaceutically acceptable salts and prodrugs thereof and pharmaceutically acceptable salts of said prodrugs.

- 5 136. The method of claim 100 wherein said phosphonic acid-containing compound is a compound of Formula II:



wherein:

- A is selected from the group consisting of $-NR^i$ -, $-O$ -, and $-S$ -;
- 10 B is selected from the group consisting of $-CR^b$ -, and $-N$ -;
- R^i is selected from the group consisting of hydrogen, $-C(O)C_1-C_4$ alkyl, $-C_1-C_4$ alkyl, and $-C_1-C_4$ -aryl;
- R^b is selected from the group consisting of hydrogen and optionally substituted $-C_1-C_4$ alkyl;
- 15 G is selected from the group consisting of $-O$ -, $-S$ -, $-S(=O)$ -, $-S(=O)_2$ -, $-CH_2$ -, $-CF_2$ -, $-CHF$ -, $-C(O)$ -, $-CH(OH)$ -, $-NH$ -, and $-N(C_1-C_4$ alkyl)-;
- D is selected from the group consisting of a bond, $-(CR^a)_2$ -, and $-C(O)$ -;
- Each R^a is independently selected from the group consisting of hydrogen, optionally substituted $-C_1-C_4$ alkyl, halogen, $-OH$, optionally substituted $-O-C_1-C_4$
- 20 alkyl, $-OCF_3$, optionally substituted $-S-C_1-C_4$ alkyl, $-NR^bR^c$, optionally substituted $-C_2-C_4$ alkenyl, and optionally substituted $-C_2-C_4$ alkynyl; with the proviso that when one R^a is attached to C through an O, S, or N atom, then the other R^a attached to the same C is a hydrogen, or attached via a carbon atom;
- R^1 and R^2 are each independently selected from the group consisting of halogen,
- 25 optionally substituted $-C_1-C_4$ alkyl, optionally substituted $-S-C_1-C_3$ alkyl, optionally substituted $-C_2-C_4$ alkenyl, optionally substituted $-C_2-C_4$ alkynyl, $-CF_3$, $-OCF_3$, optionally substituted $-O-C_1-C_3$ alkyl, and cyano;
- R^3 and R^4 are each independently selected from the group consisting of hydrogen, halogen, $-CF_3$, $-OCF_3$, cyano, optionally substituted $-C_1-C_{12}$ alkyl, optionally
- 30 substituted $-C_2-C_{12}$ alkenyl, optionally substituted $-C_2-C_{12}$ alkynyl, optionally

substituted $-(CR^a)_m$ aryl, optionally substituted $-(CR^a)_m$ cycloalkyl, optionally substituted $-(CR^a)_m$ heterocycloalkyl, $-OR^d$, $-SR^d$, $-S(=O)R^e$, $-S(=O)_2R^e$, $-S(=O)_2NR^fR^g$, $-C(O)NR^fR^g$, $-C(O)OR^h$, $-C(O)R^e$, $-N(R^b)C(O)R^e$, $-N(R^b)C(O)NR^fR^g$, $-N(R^b)S(=O)_2R^e$, $-N(R^b)S(=O)_2NR^fR^g$, and $-NR^fR^g$;

- 5 Each R^d is selected from the group consisting of optionally substituted $-C_1$ - C_{12} alkyl, optionally substituted $-C_2$ - C_{12} alkenyl, optionally substituted $-C_2$ - C_{12} alkynyl, optionally substituted $-(CR^b)_n$ aryl, optionally substituted $-(CR^b)_n$ cycloalkyl, optionally substituted $-(CR^b)_n$ heterocycloalkyl, and $-C(O)NR^fR^g$;

- Each R^e is selected from the group consisting of optionally substituted $-C_1$ - C_{12} alkyl, optionally substituted $-C_2$ - C_{12} alkenyl, optionally substituted $-C_2$ - C_{12} alkynyl, optionally substituted $-(CR^a)_n$ aryl, optionally substituted $-(CR^a)_n$ cycloalkyl, and optionally substituted $-(CR^a)_n$ heterocycloalkyl;

- R^f and R^g are each independently selected from the group consisting of hydrogen, optionally substituted $-C_1$ - C_{12} alkyl, optionally substituted $-C_2$ - C_{12} alkenyl, optionally substituted $-C_2$ - C_{12} alkynyl, optionally substituted $-(CR^b)_n$ aryl, optionally substituted $-(CR^b)_n$ cycloalkyl, and optionally substituted $-(CR^b)_n$ heterocycloalkyl, or R^f and R^g may together form an optionally substituted heterocyclic ring, which may contain a second heterogroup selected from the group consisting of O, NR^c , and S, wherein said optionally substituted heterocyclic ring may be substituted with 0-4 substituents selected from the group consisting of optionally substituted $-C_1$ - C_4 alkyl, $-OR^b$, oxo, cyano, $-CF_3$, optionally substituted phenyl, and $-C(O)OR^h$;

- Each R^h is selected from the group consisting of optionally substituted $-C_1$ - C_{12} alkyl, optionally substituted $-C_2$ - C_{12} alkenyl, optionally substituted $-C_2$ - C_{12} alkynyl, optionally substituted $-(CR^b)_n$ aryl, optionally substituted $-(CR^b)_n$ cycloalkyl, and optionally substituted $-(CR^b)_n$ heterocycloalkyl;

R^5 is selected from the group consisting of $-OH$, optionally substituted $-OC_1$ - C_6 alkyl, $-OC(O)R^e$, $-OC(O)OR^h$, $-F$, $-NHC(O)R^e$, $-NHS(=O)R^e$, $-NHS(=O)_2R^e$, $-NHC(=S)NH(R^h)$, and $-NHC(O)NH(R^h)$;

X is $P(O)YR^{11}Y'R^{11}$;

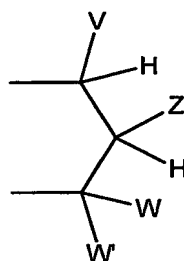
- 30 Y and Y' are each independently selected from the group consisting of $-O-$, and $-NR^v-$; when Y and Y' are $-O-$, R^{11} attached to $-O-$ is independently selected from the group consisting of $-H$, alkyl, optionally substituted aryl, optionally substituted heterocycloalkyl, optionally substituted CH_2 -heterocycloalkyl wherein the cyclic moiety contains a carbonate or thiocarbonate, optionally substituted $-alkylaryl$,

$-C(R^Z)_2OC(O)NR^Z$, $-NR^Z-C(O)-R^Y$, $-C(R^Z)_2-OC(O)R^Y$,
 $-C(R^Z)_2-O-C(O)OR^Y$, $-C(R^Z)_2OC(O)SR^Y$, -alkyl-S-C(O) R^Y , -alkyl-S-S-alkylhydroxy,
 and -alkyl-S-S-S-alkylhydroxy;

when Y and Y' are $-NR^V$ -, then R^{11} attached to $-NR^V$ - is independently selected
 5 from the group consisting
 of -H, $-[C(R^Z)_2]_q-COOR^Y$, $-C(R^X)_2COOR^Y$, $-[C(R^Z)_2]_q-C(O)SR^Y$,
 and -cycloalkylene- $COOR^Y$;

when Y is -O- and Y' is NR^V , then R^{11} attached to -O- is independently selected
 from the group consisting of -H, alkyl, optionally substituted aryl, optionally substituted
 10 heterocycloalkyl, optionally substituted CH_2 -heterocycloalkyl wherein the cyclic moiety
 contains a carbonate or thiocarbonate, optionally
 substituted -alkylaryl, $-C(R^Z)_2OC(O)NR^Z$, $-NR^Z-C(O)-R^Y$, $-C(R^Z)_2-OC(O)R^Y$,
 $-C(R^Z)_2-O-C(O)OR^Y$, $-C(R^Z)_2OC(O)SR^Y$, -alkyl-S-C(O) R^Y , -alkyl-S-S-alkylhydroxy,
 and -alkyl-S-S-S-alkylhydroxy; and R^{11} attached to $-NR^V$ - is independently selected from
 15 the group consisting of -H, $-[C(R^Z)_2]_q-COOR^Y$, $-C(R^X)_2COOR^Y$, $-[C(R^Z)_2]_q-C(O)SR^Y$,
 and -cycloalkylene- $COOR^Y$;

or when Y and Y' are independently selected from -O- and $-NR^V$ -, then together
 R^{11} and R^{11} are -alkyl-S-S-alkyl- to form a cyclic group, or together R^{11} and R^{11} are the
 group:



20

wherein:

V, W, and W' are independently selected from the group consisting of hydrogen,
 optionally substituted alkyl, optionally substituted aralkyl, heterocycloalkyl, aryl,
 substituted aryl, heteroaryl, substituted heteroaryl, optionally substituted 1-alkenyl, and
 25 optionally substituted 1-alkynyl;

or together V and Z are connected via an additional 3-5 atoms to form a cyclic
 group containing 5-7 atoms, wherein 0-1 atoms are heteroatoms and the remaining
 atoms are carbon, substituted with hydroxy, acyloxy, alkylthiocarbonyloxy,

alkoxycarbonyloxy, or aryloxycarbonyloxy attached to a carbon atom that is three atoms from both Y groups attached to the phosphorus; or

or together V and Z are connected via an additional 3-5 atoms to form a cyclic group, wherein 0-1 atoms are heteroatoms and the remaining atoms are carbon, that is fused to an aryl group at the beta and gamma position to the Y attached to the phosphorus;

or together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to one of said carbon atoms that is three atoms from a Y attached to the phosphorus;

or together Z and W are connected via an additional 3-5 atoms to form a cyclic group, wherein 0-1 atoms are heteroatoms and the remaining atoms are carbon, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

or together W and W' are connected via an additional 2-5 atoms to form a cyclic group, wherein 0-2 atoms are heteroatoms and the remaining atoms are carbon, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

Z is selected from the group consisting of $-\text{CHR}^z\text{OH}$, $-\text{CHR}^z\text{OC(O)R}^y$, $-\text{CHR}^z\text{OC(S)R}^y$, $-\text{CHR}^z\text{OC(S)OR}^y$, $-\text{CHR}^z\text{OC(O)SR}^y$, $-\text{CHR}^z\text{OCO}_2\text{R}^y$, $-\text{OR}^z$, $-\text{SR}^z$, $-\text{CHR}^z\text{N}_3$, $-\text{CH}_2\text{aryl}$, $-\text{CH(aryl)OH}$, $-\text{CH(CH=CR}^z_2)\text{OH}$, $-\text{CH(C}\equiv\text{CR}^z_2)\text{OH}$, $-\text{R}^z$, $-\text{NR}^z_2$, $-\text{OCOR}^y$, $-\text{OCO}_2\text{R}^y$, $-\text{SCOR}^y$, $-\text{SCO}_2\text{R}^y$, $-\text{NHCOR}^z$, $-\text{NHCO}_2\text{R}^y$, $-\text{CH}_2\text{NHaryl}$, $-(\text{CH}_2)_q-\text{OR}^z$, and $-(\text{CH}_2)_q-\text{SR}^z$;

q is an integer 2 or 3;

Each R^z is selected from the group consisting of R^y and $-\text{H}$;

Each R^y is selected from the group consisting of alkyl, aryl, heterocycloalkyl, and aralkyl;

Each R^x is independently selected from the group consisting of $-\text{H}$, and alkyl, or together R^x and R^x form a cyclic alkyl group;

Each R^y is selected from the group consisting of $-\text{H}$, lower alkyl, acyloxyalkyl, alkoxycarbonyloxyalkyl, and lower acyl;

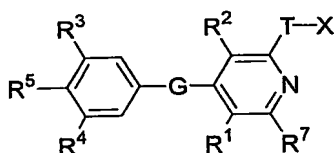
- a) V, Z, W, W' are not all $-\text{H}$; and
- b) when Z is $-\text{R}^z$, then at least one of V, W, and W' is not $-\text{H}$, alkyl, aralkyl, or heterocycloalkyl;

and pharmaceutically acceptable salts and prodrugs thereof and pharmaceutically acceptable salts of said prodrugs.

137. The method of claim 135 wherein said metabolic disease is hypercholesterolemia.

5 138. The method of claim 135 wherein said metabolic disease is obesity.

139. A compound of Formula III:



wherein:

- G is selected from the group consisting of -O-, -S-, -S(=O)-, -S(=O)₂-,
 10 -CH₂-, -CF₂-, -CHF-, -C(O)-, -CH(OH)-, -NH-, and -N(C₁-C₄ alkyl)-;
 T is selected from the group consisting of -(CR^a₂)_k-, -CR^b=CR^b-(CR^a₂)_n-,
 -(CR^a₂)_n-CR^b=CR^b-, -(CR^a₂)-CR^b=CR^b-(CR^a₂)-,
 -O(CR^b₂)(CR^a₂)_n-, -S(CR^b₂)(CR^a₂)_n-, -N(R^c)(CR^b₂)(CR^a₂)_n-, -N(R^b)C(O)(CR^a₂)_n-,
 -(CR^a₂)_nCH(NR^bR^c)-, -C(O)(CR^a₂)_m-, -(CR^a₂)_mC(O)-, -(CR^a₂)C(O)(CR^a₂)_n-,
 15 -(CR^a₂)_nC(O)(CR^a₂)-, and -C(O)NH(CR^b₂)(CR^a₂)_p-;

k is an integer from 0-4;

m is an integer from 0-3;

n is an integer from 0-2;

p is an integer from 0-1;

- 20 Each R^a is independently selected from the group consisting of hydrogen, optionally substituted -C₁-C₄ alkyl, halogen, -OH, optionally substituted -O-C₁-C₄ alkyl, -OCF₃, optionally substituted -S-C₁-C₄ alkyl, -NR^bR^c, optionally substituted -C₂-C₄ alkenyl, and optionally substituted -C₂-C₄ alkynyl; with the proviso that when one R^a is attached to C through an O, S, or N atom, then the other R^a attached
 25 to the same C is a hydrogen, or attached via a carbon atom;

Each R^b is independently selected from the group consisting of hydrogen and optionally substituted -C₁-C₄ alkyl;

Each R^c is independently selected from the group consisting of hydrogen and optionally substituted -C₁-C₄ alkyl, optionally substituted -C(O)-C₁-C₄ alkyl,
 30 and -C(O)H;

R^1 and R^2 are each independently selected from the group consisting of halogen, optionally substituted $-C_1-C_4$ alkyl, optionally substituted $-S-C_1-C_3$ alkyl, optionally substituted $-C_2-C_4$ alkenyl, optionally substituted $-C_2-C_4$ alkynyl, $-CF_3$, $-OCF_3$, optionally substituted $-O-C_1-C_3$ alkyl, and cyano;

5 R^3 and R^4 are each independently selected from the group consisting of hydrogen, halogen, $-CF_3$, $-OCF_3$, cyano, optionally substituted $-C_1-C_{12}$ alkyl, optionally substituted $-C_2-C_{12}$ alkenyl, optionally substituted $-C_2-C_{12}$ alkynyl, optionally substituted $-(CR^a_2)_m$ aryl, optionally substituted $-(CR^a_2)_m$ cycloalkyl, optionally substituted $-(CR^a_2)_m$ heterocycloalkyl, $-OR^d$, $-SR^d$, $-S(=O)R^e$, $-S(=O)_2R^e$, $-S(=O)_2NR^fR^g$,
10 $-C(O)NR^fR^g$, $-C(O)OR^h$, $-C(O)R^e$, $-N(R^b)C(O)R^e$, $-N(R^b)C(O)NR^fR^g$, $-N(R^b)S(=O)_2R^e$, $-N(R^b)S(=O)_2NR^fR^g$, and $-NR^fR^g$;

Each R^d is selected from the group consisting of optionally substituted $-C_1-C_{12}$ alkyl, optionally substituted $-C_2-C_{12}$ alkenyl, optionally substituted $-C_2-C_{12}$ alkynyl, optionally substituted $-(CR^b_2)_n$ aryl, optionally substituted $-(CR^b_2)_n$ cycloalkyl, optionally substituted $-(CR^b_2)_n$ heterocycloalkyl, and $-C(O)NR^fR^g$;

Each R^e is selected from the group consisting of optionally substituted $-C_1-C_{12}$ alkyl, optionally substituted $-C_2-C_{12}$ alkenyl, optionally substituted $-C_2-C_{12}$ alkynyl, optionally substituted $-(CR^a_2)_n$ aryl, optionally substituted $-(CR^a_2)_n$ cycloalkyl, and optionally substituted $-(CR^a_2)_n$ heterocycloalkyl;

20 R^f and R^g are each independently selected from the group consisting of hydrogen, optionally substituted $-C_1-C_{12}$ alkyl, optionally substituted $-C_2-C_{12}$ alkenyl, optionally substituted $-C_2-C_{12}$ alkynyl, optionally substituted $-(CR^b_2)_n$ aryl, optionally substituted $-(CR^b_2)_n$ cycloalkyl, and optionally substituted $-(CR^b_2)_n$ heterocycloalkyl, or R^f and R^g may together form an optionally substituted heterocyclic ring, which may contain
25 a second heterogroup selected from the group consisting of O, NR^c , and S, wherein said optionally substituted heterocyclic ring may be substituted with 0-4 substituents selected from the group consisting of optionally substituted $-C_1-C_4$ alkyl, $-OR^b$, oxo, cyano, $-CF_3$, optionally substituted phenyl, and $-C(O)OR^h$;

Each R^h is selected from the group consisting of optionally substituted $-C_1-C_{12}$ alkyl, optionally substituted $-C_2-C_{12}$ alkenyl, optionally substituted $-C_2-C_{12}$ alkynyl, optionally substituted $-(CR^b_2)_n$ aryl, optionally substituted $-(CR^b_2)_n$ cycloalkyl, and optionally substituted $-(CR^b_2)_n$ heterocycloalkyl;

R^5 is selected from the group consisting of -OH, optionally substituted -OC₁-C₆ alkyl, -OC(O)R^e, -OC(O)OR^h, -F, -NHC(O)R^e, -NHS(=O)R^e, -NHS(=O)₂R^e, -NHC(=S)NH(R^h), and -NHC(O)NH(R^h);

R^7 is selected from the group consisting of hydrogen, halogen, amino, hydroxyl, -O-C₁-C₄ alkyl, -SH and -S-C₁-C₄ alkyl;

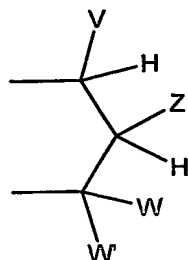
X is P(O)YR¹¹Y'R¹¹;

Y and Y' are each independently selected from the group consisting of -O-, and -NR^v-; when Y and Y' are -O-, R¹¹ attached to -O- is independently selected from the group consisting of -H, alkyl, optionally substituted aryl, optionally substituted heterocycloalkyl, optionally substituted CH₂-heterocycloalkyl wherein the cyclic moiety contains a carbonate or thiocarbonate, optionally substituted -alkylaryl, -C(R^z)₂OC(O)NR^z₂, -NR^z-C(O)-R^y, -C(R^z)₂-OC(O)R^y, -C(R^z)₂-O-C(O)OR^y, -C(R^z)₂OC(O)SR^y, -alkyl-S-C(O)R^y, -alkyl-S-S-alkylhydroxy, and -alkyl-S-S-S-alkylhydroxy;

when Y and Y' are -NR^v-, then R¹¹ attached to -NR^v- is independently selected from the group consisting of -H, -[C(R^z)₂]_q-COOR^y, -C(R^x)₂COOR^y, -[C(R^z)₂]_q-C(O)SR^y, and -cycloalkylene-COOR^y;

when Y is -O- and Y' is NR^v-, then R¹¹ attached to -O- is independently selected from the group consisting of -H, alkyl, optionally substituted aryl, optionally substituted heterocycloalkyl, optionally substituted CH₂-heterocycloalkyl wherein the cyclic moiety contains a carbonate or thiocarbonate, optionally substituted -alkylaryl, -C(R^z)₂OC(O)NR^z₂, -NR^z-C(O)-R^y, -C(R^z)₂-OC(O)R^y, -C(R^z)₂-O-C(O)OR^y, -C(R^z)₂OC(O)SR^y, -alkyl-S-C(O)R^y, -alkyl-S-S-alkylhydroxy, and -alkyl-S-S-S-alkylhydroxy; and R¹¹ attached to -NR^v- is independently selected from the group consisting of -H, -[C(R^z)₂]_q-COOR^y, -C(R^x)₂COOR^y, -[C(R^z)₂]_q-C(O)SR^y, and -cycloalkylene-COOR^y;

or when Y and Y' are independently selected from -O- and -NR^v-, then together R¹¹ and R¹¹ are -alkyl-S-S-alkyl- to form a cyclic group, or together R¹¹ and R¹¹ are the group:



wherein:

V, W, and W' are independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted aralkyl, heterocycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, optionally substituted 1-alkenyl, and optionally substituted 1-alkynyl;

or together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 atoms, wherein 0-1 atoms are heteroatoms and the remaining atoms are carbon, substituted with hydroxy, acyloxy, alkylthiocarbonyloxy, alkoxy, alkoxy, or aryloxy, or aryloxy attached to a carbon atom that is three atoms from both Y groups attached to the phosphorus; or

or together V and Z are connected via an additional 3-5 atoms to form a cyclic group, wherein 0-1 atoms are heteroatoms and the remaining atoms are carbon, that is fused to an aryl group at the beta and gamma position to the Y attached to the phosphorus;

or together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxy, alkoxy, alkylthiocarbonyloxy, and aryloxy, attached to one of said carbon atoms that is three atoms from a Y attached to the phosphorus;

or together Z and W are connected via an additional 3-5 atoms to form a cyclic group, wherein 0-1 atoms are heteroatoms and the remaining atoms are carbon, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

or together W and W' are connected via an additional 2-5 atoms to form a cyclic group, wherein 0-2 atoms are heteroatoms and the remaining atoms are carbon, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

Z is selected from the group consisting of $-\text{CHR}^Z\text{OH}$, $-\text{CHR}^Z\text{OC(O)R}^Y$, $-\text{CHR}^Z\text{OC(S)R}^Y$, $-\text{CHR}^Z\text{OC(S)OR}^Y$, $-\text{CHR}^Z\text{OC(O)SR}^Y$, $-\text{CHR}^Z\text{OCO}_2\text{R}^Y$, $-\text{OR}^Z$,

-SR^z, -CHR^zN₃, -CH₂aryl, -CH(aryl)OH, -CH(CH=CR^z)OH, -CH(C≡CR^z)OH, -R^z, -NR^z, -OCOR^y, -OCO₂R^y, -SCOR^y, -SCO₂R^y, -NHCOR^z, -NHCO₂R^y, -CH₂NHaryl, -(CH₂)_q-OR^z, and -(CH₂)_q-SR^z;

q is an integer 2 or 3;

5 Each R^z is selected from the group consisting of R^y and -H;

Each R^y is selected from the group consisting of alkyl, aryl, heterocycloalkyl, and aralkyl;

Each R^x is independently selected from the group consisting of -H, and alkyl, or together R^x and R^x form a cyclic alkyl group;

10 Each R^v is selected from the group consisting of -H, lower alkyl, acyloxyalkyl, alkoxy-carbonyloxyalkyl, and lower acyl;

with the provisos that:

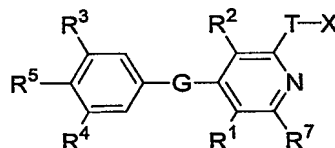
a) when G is -O-, T is -NH-CH₂-, R¹ and R² are each chloro, R³ is *iso*-propyl, R⁴ is hydrogen, R⁷ is fluoro, and R⁵ is -OH, then X is not P(O)(OH)₂,
15 P(O)(OH)(OCH₃) or P(O)(OCH₃)₂;

b) V, Z, W, W' are not all -H; and

c) when Z is -R^z, then at least one of V, W, and W' is not -H, alkyl, aralkyl, or heterocycloalkyl;

and pharmaceutically acceptable salts and prodrugs thereof and pharmaceutically
20 acceptable salts of said prodrugs.

140. A compound of Formula III:



wherein:

G is selected from the group consisting of -O-, -S-, -S(=O)-, -S(=O)₂-,
25 -CH₂-, -CF₂-, -CHF-, -C(O)-, -CH(OH)-, -NH-, and -N(C₁-C₄ alkyl)-;
T is selected from the group consisting of -(CR^a)_k-, -CR^b=CR^b-(CR^a)_n-,
-(CR^a)_n-CR^b=CR^b-, -(CR^a)_n-CR^b=CR^b-(CR^a)_n-,
-O(CR^b)₂(CR^a)_n-, -S(CR^b)₂(CR^a)_n-, -N(R^c)(CR^b)₂(CR^a)_n-, -N(R^b)C(O)(CR^a)_n-,
-(CR^a)_nCH(NR^bR^c)-, -C(O)(CR^a)_m-, -(CR^a)_mC(O)-, -(CR^a)C(O)(CR^a)_n-,
30 -(CR^a)_nC(O)(CR^a)_n-, and -C(O)NH(CR^b)₂(CR^a)_p-;

k is an integer from 0-4;

m is an integer from 0-3;

n is an integer from 0-2;

p is an integer from 0-1;

5 Each R^a is independently selected from the group consisting of hydrogen, optionally substituted $-C_1-C_4$ alkyl, halogen, $-OH$, optionally substituted $-O-C_1-C_4$ alkyl, $-OCF_3$, optionally substituted $-S-C_1-C_4$ alkyl, $-NR^bR^c$, optionally substituted $-C_2-C_4$ alkenyl, and optionally substituted $-C_2-C_4$ alkynyl; with the proviso that when one R^a is attached to C through an O, S, or N atom, then the other R^a attached
10 to the same C is a hydrogen, or attached via a carbon atom;

Each R^b is independently selected from the group consisting of hydrogen and optionally substituted $-C_1-C_4$ alkyl;

Each R^c is independently selected from the group consisting of hydrogen, optionally substituted $-C_1-C_4$ alkyl, optionally substituted $-C(O)-C_1-C_4$ alkyl,
15 and $-C(O)H$;

R^1 and R^2 are each independently selected from the group consisting of halogen, optionally substituted $-C_1-C_4$ alkyl, optionally substituted $-S-C_1-C_3$ alkyl, optionally substituted $-C_2-C_4$ alkenyl, optionally substituted $-C_2-C_4$ alkynyl, $-CF_3$, $-OCF_3$, optionally substituted $-O-C_1-C_3$ alkyl, and cyano;

20 R^3 and R^4 are each independently selected from the group consisting of hydrogen, halogen, $-CF_3$, $-OCF_3$, cyano, optionally substituted $-C_1-C_{12}$ alkyl, optionally substituted $-C_2-C_{12}$ alkenyl, optionally substituted $-C_2-C_{12}$ alkynyl, optionally substituted $-(CR^a)_m$ aryl, optionally substituted $-(CR^a)_m$ cycloalkyl, optionally substituted $(CR^a)_m$ heterocycloalkyl, $-OR^d$, $-SR^d$, $-S(=O)R^e$, $-S(=O)_2R^e$, $-S(=O)_2NR^fR^g$, $-C(O)NR^fR^g$,
25 $-C(O)OR^h$, $-C(O)R^e$, $-N(R^b)C(O)R^e$, $-N(R^b)C(O)NR^fR^g$, $-N(R^b)S(=O)_2R^e$, $-N(R^b)S(=O)_2NR^fR^g$, and $-NR^fR^g$;

Each R^d is selected from the group consisting of optionally substituted $-C_1-C_{12}$ alkyl, optionally substituted $-C_2-C_{12}$ alkenyl, optionally substituted $-C_2-C_{12}$ alkynyl, optionally substituted $-(CR^b)_n$ aryl, optionally substituted $-(CR^b)_n$ cycloalkyl, optionally substituted $-(CR^b)_n$ heterocycloalkyl, and $-C(O)NR^fR^g$;
30

Each R^e is optionally substituted $-C_1-C_{12}$ alkyl, optionally substituted $-C_2-C_{12}$ alkenyl, optionally substituted $-C_2-C_{12}$ alkynyl, optionally substituted $-(CR^a)_n$ aryl, optionally substituted $-(CR^a)_n$ cycloalkyl, and optionally substituted $-(CR^a)_n$ heterocycloalkyl;

R^f and R^g are each independently selected from the group consisting of hydrogen, optionally substituted $-C_1-C_{12}$ alkyl, optionally substituted $-C_2-C_{12}$ alkenyl, optionally substituted $-C_2-C_{12}$ alkynyl, optionally substituted $-(CR^b)_n$ aryl, optionally substituted $-(CR^b)_n$ cycloalkyl, and optionally substituted $-(CR^b)_n$ heterocycloalkyl, or R^f and R^g may together form an optionally substituted heterocyclic ring, which may contain a second heterogroup selected from the group of O, NR^c , and S, wherein said optionally substituted heterocyclic ring may be substituted with 0-4 substituents selected from the group consisting of optionally substituted $-C_1-C_4$ alkyl, $-OR^b$, oxo, cyano, $-CF_3$, optionally substituted phenyl, and $-C(O)OR^h$;

Each R^h is selected from the group consisting of optionally substituted $-C_1-C_{12}$ alkyl, optionally substituted $-C_2-C_{12}$ alkenyl, optionally substituted $-C_2-C_{12}$ alkynyl, optionally substituted $-(CR^b)_n$ aryl, optionally substituted $-(CR^b)_n$ cycloalkyl, and optionally substituted $-(CR^b)_n$ heterocycloalkyl;

R^5 is selected from the group consisting of $-OH$, optionally substituted $-OC_1-C_6$ alkyl, $-OC(O)R^e$, $-OC(O)OR^h$, $-F$, $-NHC(O)R^e$, $-NHS(=O)R^e$, $-NHS(=O)_2R^e$, $-NHC(=S)NH(R^h)$, and $-NHC(O)NH(R^h)$;

R^7 is selected from the group consisting of hydrogen, halogen, amino, hydroxyl, $-O-C_1-C_4$ alkyl, $-SH$ and $-S-C_1-C_4$ alkyl;

X is $P(O)YR^{11}Y'R^{11}$;

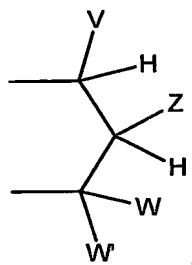
Y and Y' are each independently selected from the group consisting of $-O-$, and $-NR^v-$; when Y and Y' are $-O-$, R^{11} attached to $-O-$ is independently selected from the group consisting of $-H$, alkyl, optionally substituted aryl, optionally substituted heterocycloalkyl, optionally substituted CH_2 -heterocycloalkyl wherein the cyclic moiety contains a carbonate or thiocarbonate, optionally substituted $-alkylaryl$, $-C(R^z)_2OC(O)NR^z$, $-NR^z-C(O)-R^y$, $-C(R^z)_2-OC(O)R^y$, $-C(R^z)_2-O-C(O)OR^y$, $-C(R^z)_2OC(O)SR^y$, $-alkyl-S-C(O)R^y$, $-alkyl-S-S-alkylhydroxy$, and $-alkyl-S-S-S-alkylhydroxy$;

when Y and Y' are $-NR^v-$, then R^{11} attached to $-NR^v-$ is independently selected from the group consisting of $-H$, $-[C(R^z)_2]_q-COOR^y$, $-C(R^x)_2COOR^y$, $-[C(R^z)_2]_q-C(O)SR^y$, and $-cycloalkylene-COOR^y$;

when Y is $-O-$ and Y' is NR^v , then R^{11} attached to $-O-$ is independently selected from the group consisting of $-H$, alkyl, optionally substituted aryl, optionally substituted heterocycloalkyl, optionally substituted CH_2 -heterocycloalkyl wherein the cyclic moiety

contains a carbonate or thiocarbonate, optionally substituted -alkylaryl, $-C(R^z)_2OC(O)NR^z$, $-NR^z-C(O)-R^y$, $-C(R^z)_2-OC(O)R^y$, $-C(R^z)_2-O-C(O)OR^y$, $-C(R^z)_2OC(O)SR^y$, -alkyl-S-C(O) R^y , -alkyl-S-S-alkylhydroxy, and -alkyl-S-S-S-alkylhydroxy; and R^{11} attached to $-NR^y$ is independently selected from the group consisting of -H, $-[C(R^z)_2]_q-COOR^y$, $-C(R^x)_2COOR^y$, $-[C(R^z)_2]_q-C(O)SR^y$, and -cycloalkylene- $COOR^y$;

or when Y and Y' are independently selected from -O- and $-NR^y$ -, then together R^{11} and R^{11} are -alkyl-S-S-alkyl- to form a cyclic group, or together R^{11} and R^{11} are the group:



wherein:

V, W, and W' are independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted aralkyl, heterocycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, optionally substituted 1-alkenyl, and optionally substituted 1-alkynyl;

or together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 atoms, wherein 0 – 1 atoms are heteroatoms and the remaining atoms are carbon, substituted with hydroxy, acyloxy, alkylthiocarbonyloxy, alkoxycarbonyloxy, or aryloxycarbonyloxy attached to a carbon atom that is three atoms from both Y groups attached to the phosphorus; or

or together V and Z are connected via an additional 3-5 atoms to form a cyclic group, wherein 0–1 atoms are heteroatoms and the remaining atoms are carbon, that is fused to an aryl group at the beta and gamma position to the Y attached to the phosphorus;

or together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy,

alkylthiocarbonyloxy, and aryloxy carbonyloxy, attached to one of said carbon atoms that is three atoms from a Y attached to the phosphorus;

or together Z and W are connected via an additional 3-5 atoms to form a cyclic group, wherein 0-1 atoms are heteroatoms and the remaining atoms are carbon, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

or together W and W' are connected via an additional 2-5 atoms to form a cyclic group, wherein 0-2 atoms are heteroatoms and the remaining atoms are carbon, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

Z is selected from the group consisting of $-\text{CHR}^z\text{OH}$, $-\text{CHR}^z\text{OC(O)}\text{R}^y$, $-\text{CHR}^z\text{OC(S)}\text{R}^y$, $-\text{CHR}^z\text{OC(S)}\text{OR}^y$, $-\text{CHR}^z\text{OC(O)}\text{SR}^y$, $-\text{CHR}^z\text{OCO}_2\text{R}^y$, $-\text{OR}^z$, $-\text{SR}^z$, $-\text{CHR}^z\text{N}_3$, $-\text{CH}_2\text{aryl}$, $-\text{CH(aryl)OH}$, $-\text{CH(CH=CR}^z_2)\text{OH}$, $-\text{CH(C}\equiv\text{CR}^z_2)\text{OH}$, $-\text{R}^z$, $-\text{NR}^z_2$, $-\text{OCOR}^y$, $-\text{OCO}_2\text{R}^y$, $-\text{SCOR}^y$, $-\text{SCO}_2\text{R}^y$, $-\text{NHCOR}^z$, $-\text{NHCO}_2\text{R}^y$, $-\text{CH}_2\text{NHaryl}$, $-(\text{CH}_2)_q-\text{OR}^z$, and $-(\text{CH}_2)_q-\text{SR}^z$;

q is an integer 2 or 3;

Each R^z is selected from the group consisting of R^y and $-\text{H}$;

Each R^y is selected from the group consisting of alkyl, aryl, heterocycloalkyl, and aralkyl;

Each R^x is independently selected from the group consisting of $-\text{H}$, and alkyl, or together R^x and R^x form a cyclic alkyl group;

Each R^v is selected from the group consisting of $-\text{H}$, lower alkyl, acyloxyalkyl, alkoxy carbonyloxyalkyl, and lower acyl;

with the provisos that:

a) when G is selected from the group consisting of $-\text{O}-$, $-\text{S}-$, $-\text{S(=O)}-$, $-\text{S(=O)}_2-$, $-\text{CH}_2-$, $-\text{C(O)}-$ and $-\text{NR}^b-$; T is $-\text{A-B}-$ where A is selected from the group consisting of $-\text{NR}^b-$, $-\text{O}-$, $-\text{CH}_2-$ and $-\text{S}-$ and B is selected from the group consisting of a bond and substituted or unsubstituted C_1-C_3 alkyl; R^3 is selected from the group consisting of halogen, trifluoromethyl, substituted or unsubstituted C_1-C_6 alkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, aryloxy, substituted amide, sulfone, sulfonamide and C_3-C_7 cycloalkyl, wherein said aryl, heteroaryl or cycloalkyl ring(s) are attached or fused to the aromatic; R^4 is selected from the group consisting of hydrogen, halogen, substituted or unsubstituted C_1-C_6 alkyl, substituted or unsubstituted aryl, and substituted or unsubstituted heteroaryl; R^1 and R^2 are each independently selected from the group consisting of halogen, substituted or unsubstituted C_1-C_4 alkyl,

and substituted or unsubstituted C₃-C₅ cycloalkyl; R⁷ is selected from the group consisting of hydrogen, halogen, amino, hydroxyl, -O-C₁-C₄ alkyl, -SH and -S-C₁-C₄ alkyl; and R⁵ is selected from the group consisting of hydroxyl, optionally substituted -OC₁-C₆ alkyl, and -OC(O)R^e; then X is not -P(O)(OH)₂;

- 5 b) V, Z, W, W' are not all -H; and
 c) when Z is -R^z, then at least one of V, W, and W' is not -H, alkyl, aralkyl, or heterocycloalkyl;

and pharmaceutically acceptable salts and prodrugs thereof and pharmaceutically acceptable salts of said prodrugs.

- 10 141. The compound of claim 139 wherein when G is -O-, T is -NH-CH₂-, R¹ and R² are each chloro, R³ is *iso*-propyl, R⁷ is fluoro and R⁵ is -OH, then R⁴ is not hydrogen.

142. The compound of claim 140 wherein when G is selected from the group consisting of oxygen, sulfur, sulfoxide, sulfonyl, -CH₂-, -C(O)- and -NR^b-; T is -A-B-
 15 where A is selected from the group consisting of -NR^b-, -O-, -CH₂- and -S- and B is selected from the group consisting of a bond and substituted or unsubstituted C₁-C₃ alkyl; R³ is selected from the group consisting of halogen, trifluoromethyl, substituted or unsubstituted C₁-C₆ alkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, aryloxy, substituted amide, sulfone, sulfonamide and C₃-C₇ cycloalkyl,
 20 wherein said aryl, heteroaryl or cycloalkyl ring(s) are attached or fused to the aromatic; R⁴ is selected from the group consisting of hydrogen, halogen, substituted or unsubstituted C₁-C₆ alkyl, substituted or unsubstituted aryl, and substituted or unsubstituted heteroaryl; R¹ and R² are each independently selected from the group consisting of halogen, substituted or unsubstituted C₁-C₄ alkyl, and substituted or
 25 unsubstituted C₃-C₅ cycloalkyl; and R⁷ is selected from the group consisting of hydrogen, halogen, amino, hydroxyl, -O-C₁-C₄ alkyl, -SH and -S-C₁-C₄ alkyl; then R⁵ is not hydroxyl, optionally substituted -OC₁-C₆ alkyl, or -OC(O)R^e.

143. The compound of claim 139 wherein G is selected from the group
 30 consisting of -O- and -CH₂-.

144. The compound of claim 140 wherein G is selected from the group consisting of -O- and -CH₂-.

145. The compound of claim 139 wherein T is selected from the group consisting of $-(CR^a_2)_n-$, $-O(CR^b_2)(CR^a_2)_p-$, $-N(R^c)(CR^b_2)(CR^a_2)_p-$, $-S(CR^b_2)(CR^a_2)_p-$, $-NR^b(CO)-$, and $-CH_2CH(NR^cR^b)-$.

146. The compound of claim 140 wherein T is selected from the group
5 consisting of $-(CR^a_2)_n-$, $-O(CR^b_2)(CR^a_2)_p-$, $-N(R^c)(CR^b_2)(CR^a_2)_p-$, $-S(CR^b_2)(CR^a_2)_p-$, $-NR^b(CO)-$, and $-CH_2CH(NR^cR^b)-$.

147. The compound of claim 139 wherein R^1 and R^2 are the same and are selected from the group consisting of halogen, $-C_1-C_4$ alkyl, $-CF_3$, and cyano.

148. The compound of claim 140 wherein R^1 and R^2 are the same and are
10 selected from the group consisting of halogen, $-C_1-C_4$ alkyl, $-CF_3$, and cyano.

149. The compound of claim 139 wherein R^1 and R^2 are different and are selected from the group consisting of halogen, $-C_1-C_4$ alkyl, $-CF_3$, and cyano.

150. The compound of claim 140 wherein R^1 and R^2 are different and are selected from the group consisting of halogen, $-C_1-C_4$ alkyl, $-CF_3$, and cyano.

151. The compound of claim 139 wherein R^4 is selected from the group consisting of hydrogen, halogen, $-C_1-C_4$ alkyl, cyano and CF_3 .

152. The compound of claim 140 wherein R^4 is selected from the group consisting of hydrogen, halogen, $-C_1-C_4$ alkyl, cyano, and CF_3 .

153. The compound of claim 139 wherein R^5 is selected from the group
20 consisting of $-OH$, $-OC(O)R^e$, $-OC(O)OR^h$, $-F$, and $-NHC(O)R^e$.

154. The compound of claim 140 wherein R^5 is selected from the group consisting of $-OH$, $-OC(O)R^e$, $-OC(O)OR^h$, $-F$, and $-NHC(O)R^e$.

155. The compound of claim 139 wherein R^3 is selected from the group consisting of halogen, optionally substituted $-C_1-C_6$ alkyl, $-CF_3$, cyano, $-C(O)NR^fR^g$,
25 optionally substituted $-(CR^a_2)_n$ aryl, $-SO_2NR^fR^g$, and $-SO_2R^e$.

156. The compound of claim 140 wherein R^3 is selected from the group consisting of halogen, optionally substituted $-C_1-C_6$ alkyl, $-CF_3$, cyano, $-C(O)NR^fR^g$, optionally substituted $-(CR^a_2)_n$ aryl, $-SO_2NR^fR^g$, and $-SO_2R^e$.

157. The compound of claim 139 wherein X is selected from the group
30 consisting of $-PO_3H_2$, $-P(O)[-OCR^z_2OC(O)R^y]_2$, $-P(O)[-OCR^z_2OC(O)OR^y]_2$, $-P(O)[-N(H)CR^z_2C(O)OR^y]_2$, $-P(O)[-N(H)CR^z_2C(O)OR^y][-OR^{11}]$, and $-P(O)[-OCH(V)CH_2CH_2O-]$, wherein V is selected from the group consisting of optionally substituted aryl, aryl, heteroaryl, and optionally substituted heteroaryl.

158. The compound of claim 140 wherein X is selected from the group consisting of $-\text{PO}_3\text{H}_2$, $-\text{P}(\text{O})[-\text{OCR}^z\text{OC}(\text{O})\text{R}^y]_2$, $-\text{P}(\text{O})[-\text{OCR}^z\text{OC}(\text{O})\text{OR}^y]_2$, $-\text{P}(\text{O})[-\text{N}(\text{H})\text{CR}^z\text{C}(\text{O})\text{OR}^y]_2$, $-\text{P}(\text{O})[-\text{N}(\text{H})\text{CR}^z\text{C}(\text{O})\text{OR}^y][-\text{OR}^{11}]$, and $-\text{P}(\text{O})[-\text{OCH}(\text{V})\text{CH}_2\text{CH}_2\text{O}-]$, wherein V is selected from the group consisting of optionally substituted aryl, aryl, heteroaryl, and optionally substituted heteroaryl.

159. The compound of claim 139 wherein R^7 is selected from the group consisting of hydrogen, fluoro, chloro, amino, hydroxyl, and $-\text{O}-\text{CH}_3$.

160. The compound of claim 140 wherein R^7 is selected from the group consisting of hydrogen, fluoro, chloro, amino, hydroxyl, and $-\text{O}-\text{CH}_3$.

161. The compound of claim 139 wherein G is selected from the group consisting of $-\text{O}-$ and $-\text{CH}_2-$; T is selected from the group consisting of $-(\text{CR}^a_2)_n-$, $-\text{O}(\text{CR}^b_2)(\text{CR}^a_2)_p-$, $-\text{N}(\text{R}^c)(\text{CR}^b_2)(\text{CR}^a_2)_p-$, $-\text{S}(\text{CR}^b_2)(\text{CR}^a_2)_p-$, $-\text{NR}^b(\text{CO})-$, and $-\text{CH}_2\text{CH}(\text{NR}^c\text{R}^b)-$; R^1 and R^2 are each independently selected from the group consisting of halogen, $-\text{C}_1$ - C_4 alkyl, $-\text{CF}_3$, and cyano; R^4 is selected from the group consisting of hydrogen, halogen, $-\text{C}_1$ - C_4 alkyl, cyano and CF_3 ; R^5 is selected from the group consisting of $-\text{OH}$, $-\text{OC}(\text{O})\text{R}^e$, $-\text{OC}(\text{O})\text{OR}^h$, $-\text{F}$, and $-\text{NHC}(\text{O})\text{R}^e$; R^3 is selected from the group consisting of halogen, optionally substituted $-\text{C}_1$ - C_6 alkyl, $-\text{CF}_3$, cyano, $-\text{C}(\text{O})\text{NR}^f\text{R}^g$, optionally substituted $-(\text{CR}^a_2)_n\text{aryl}$, $-\text{SO}_2\text{NR}^f\text{R}^g$, and $-\text{SO}_2\text{R}^e$; R^7 is selected from the group consisting of hydrogen, fluoro, chloro, amino, hydroxyl, and $-\text{O}-\text{CH}_3$; and X is selected from the group consisting

of $-\text{PO}_3\text{H}_2$, $-\text{P}(\text{O})[-\text{OCR}^z\text{OC}(\text{O})\text{R}^y]_2$, $-\text{P}(\text{O})[-\text{OCR}^z\text{OC}(\text{O})\text{OR}^y]_2$, $-\text{P}(\text{O})[-\text{N}(\text{H})\text{CR}^z\text{C}(\text{O})\text{OR}^y]_2$, $-\text{P}(\text{O})[-\text{N}(\text{H})\text{CR}^z\text{C}(\text{O})\text{OR}^y][-\text{OR}^{11}]$ and $-\text{P}(\text{O})[-\text{OCH}(\text{V})\text{CH}_2\text{CH}_2\text{O}-]$, wherein V is selected from the group consisting of optionally substituted aryl, aryl, heteroaryl, and optionally substituted heteroaryl.

162. The compound of claim 161 wherein when G is $-\text{O}-$, T is $-\text{CH}_2-$, R^1 and R^2 are chloro, R^3 is *iso*-propyl, R^7 is fluoro, and R^5 is $-\text{OH}$, then R^4 is not hydrogen.

163. The compound of claim 140 wherein G is selected from the group consisting of $-\text{O}-$ and $-\text{CH}_2-$; T is selected from the group consisting of $-(\text{CR}^a_2)_n-$, $-\text{O}(\text{CR}^b_2)(\text{CR}^a_2)_p-$, $-\text{N}(\text{R}^c)(\text{CR}^b_2)(\text{CR}^a_2)_p-$, $-\text{S}(\text{CR}^b_2)(\text{CR}^a_2)_p-$, $-\text{NR}^b(\text{CO})-$, and $-\text{CH}_2\text{CH}(\text{NR}^c\text{R}^b)-$; R^1 and R^2 are each independently selected from the group consisting of halogen, $-\text{C}_1$ - C_4 alkyl, $-\text{CF}_3$, and cyano; R^4 is selected from the group consisting of hydrogen, halogen, $-\text{C}_1$ - C_4 alkyl, cyano, and CF_3 ; R^5 is selected from the group consisting of $-\text{OH}$, $-\text{OC}(\text{O})\text{R}^e$, $-\text{OC}(\text{O})\text{OR}^h$, $-\text{F}$, and $-\text{NHC}(\text{O})\text{R}^e$; R^3 is selected

from the group consisting of halogen, optionally substituted $-C_1-C_6$ alkyl, $-CF_3$, cyano, $-C(O)NR^fR^g$, optionally substituted $(CR^a_2)_n$ aryl, $-SO_2NR^fR^g$, and $-SO_2R^e$; R^7 is selected from the group consisting of hydrogen, fluoro, chloro, amino, hydroxyl, and $-O-CH_3$, and X is selected from the group consisting

- 5 of $-PO_3H_2$, $-P(O)[-OCR^z_2OC(O)R^y]_2$, $-P(O)[-OCR^z_2OC(O)OR^y]_2$, $-P(O)[-N(H)CR^z_2C(O)OR^y]_2$, $-P(O)[-N(H)CR^z_2C(O)OR^y][-OR^{11}]$, and $-P(O)[-OCH(V)CH_2CH_2O-]$, wherein V is selected from the group consisting of optionally substituted aryl, aryl, heteroaryl, and optionally substituted heteroaryl.

164. The compound of claim 163 wherein when G is selected from the group consisting of $-O-$ and $-CH_2-$; T is $-A-B-$ where A is selected from the group consisting of $-NR^b-$, $-O-$, $-CH_2-$ and $-S-$ and B is selected from the group consisting of a bond and substituted or unsubstituted C_1-C_3 alkyl; R^3 is selected from the group consisting of halogen, trifluoromethyl, substituted or unsubstituted C_1-C_6 alkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, aryloxy, substituted amide, sulfone, sulfonamide and C_3-C_7 cycloalkyl, wherein said aryl, heteroaryl or cycloalkyl ring(s) are attached or fused to the aromatic; R^4 is selected from the group consisting of hydrogen, halogen, and substituted or unsubstituted C_1-C_4 alkyl; R^1 and R^2 are each independently selected from the group consisting of halogen and substituted or unsubstituted $-C_1-C_4$ alkyl; and R^7 is selected from the group consisting of hydrogen, fluoro, chloro, amino, hydroxyl, and $-O-CH_3$; then R^5 is not hydroxyl, optionally substituted $-OC_1-C_6$ alkyl, or $-OC(O)R^e$.
- 15 20

165. The compound of claim 161 wherein T is $-N(H)C(O)-$; R^1 and R^2 are each independently selected from the group consisting of iodo, bromo, chloro, methyl, and cyano; R^4 is selected from the group consisting of hydrogen and iodo; R^5 is selected from the group consisting of $-OH$ and $-OC(O)R^e$; R^3 is selected from the group consisting of iodo, bromo, optionally substituted $-C_1-C_6$ alkyl, optionally substituted $-CH_2$ aryl, optionally substituted $-CH(OH)$ aryl, $-C(O)$ -amido, $-S(=O)_2$ -amido, wherein the amido group is selected from the group consisting of phenethylamino, piperidinyl, 4-methylpiperizinyl, morpholinyl, cyclohexylamino, anilinyl, and indolinyl, and $-SO_2R^e$ wherein R^e is selected from the group consisting of phenyl, 4-chlorophenyl, 4-fluorophenyl, and 4-pyridyl; and R^7 is selected from the group consisting of hydrogen and fluoro.
- 25 30

166. The compound of claim 165 wherein G is $-O-$; R^1 and R^2 are each chloro; R^4 is hydrogen; R^5 is $-OH$; R^7 is fluoro; and R^3 is *iso*-propyl.

167. The compound of claim 166 wherein X is selected from the group consisting of $-\text{PO}_3\text{H}_2$, $-\text{P}(\text{O})[-\text{OCH}_2\text{OC}(\text{O})-t\text{-butyl}]_2$, $-\text{P}(\text{O})[-\text{OCH}_2\text{OC}(\text{O})O-i\text{-propyl}]_2$, $-\text{P}(\text{O})[-\text{N}(\text{H})\text{CH}(\text{CH}_3)\text{C}(\text{O})\text{OCH}_2\text{CH}_3]_2$, $-\text{P}(\text{O})[-\text{N}(\text{H})\text{C}(\text{CH}_3)_2\text{C}(\text{O})\text{OCH}_2\text{CH}_3]_2$, $-\text{P}(\text{O})[-\text{N}(\text{H})\text{CH}(\text{CH}_3)\text{C}(\text{O})\text{OCH}_2\text{CH}_3][3,4\text{-methylenedioxyphenyl}]$,
 5 $-\text{P}(\text{O})[-\text{N}(\text{H})\text{C}(\text{CH}_3)_2\text{C}(\text{O})\text{OCH}_2\text{CH}_3][3,4\text{-methylenedioxyphenyl}]$, and $-\text{P}(\text{O})[-\text{OCH}(3\text{-chlorophenyl})\text{CH}_2\text{CH}_2\text{O}-]$.

168. The compound of claim 161 wherein T is $-\text{OCH}_2-$; R^1 and R^2 are each independently selected from the group consisting of iodo, bromo, chloro, methyl, and cyano; R^4 is selected from the group consisting of hydrogen and iodo; R^5 is selected from
 10 the group consisting of $-\text{OH}$, and $-\text{OC}(\text{O})\text{R}^e$; R^3 is selected from the group consisting of iodo, bromo, optionally substituted $\text{C}_1\text{-C}_6$ alkyl, optionally substituted $-\text{CH}_2\text{aryl}$, optionally substituted $-\text{CH}(\text{OH})\text{aryl}$, $-\text{C}(\text{O})\text{-amido}$, $-\text{S}(=\text{O})_2\text{-amido}$, wherein the amido group is selected from the group consisting of phenethylamino, piperidinyl, 4-methylpiperizinyl, morpholinyl, cyclohexylamino, anilinyl, and indolinyl, and $-\text{SO}_2\text{R}^e$
 15 wherein R^e is selected from the group consisting of phenyl, 4-chlorophenyl, 4-fluorophenyl, and 4-pyridyl; and R^7 is selected from the group consisting of hydrogen and fluoro.

169. The compound of claim 168 wherein G is $-\text{O}-$; R^1 and R^2 are each chloro; R^4 is hydrogen; R^7 is fluoro; R^5 is $-\text{OH}$; and R^3 is *iso*-propyl.

20 170. The compound of claim 169 wherein X is selected from the group consisting of $-\text{PO}_3\text{H}_2$, $-\text{P}(\text{O})[-\text{OCH}_2\text{OC}(\text{O})-t\text{-butyl}]_2$, $-\text{P}(\text{O})[-\text{OCH}_2\text{OC}(\text{O})O-i\text{-propyl}]_2$, $-\text{P}(\text{O})[-\text{N}(\text{H})\text{CH}(\text{CH}_3)\text{C}(\text{O})\text{OCH}_2\text{CH}_3]_2$, $-\text{P}(\text{O})[-\text{N}(\text{H})\text{C}(\text{CH}_3)_2\text{C}(\text{O})\text{OCH}_2\text{CH}_3]_2$, $-\text{P}(\text{O})[-\text{N}(\text{H})\text{CH}(\text{CH}_3)\text{C}(\text{O})\text{OCH}_2\text{CH}_3][3,4\text{-methylenedioxyphenyl}]$, $-\text{P}(\text{O})[-\text{N}(\text{H})\text{C}(\text{CH}_3)_2\text{C}(\text{O})\text{OCH}_2\text{CH}_3][3,4\text{-methylenedioxyphenyl}]$,
 25 and $-\text{P}(\text{O})[-\text{OCH}(3\text{-chlorophenyl})\text{CH}_2\text{CH}_2\text{O}-]$.

171. The compound of claim 161 wherein T is $-\text{CH}_2-$; R^1 and R^2 are each independently selected from the group consisting of iodo, bromo, chloro, methyl, and cyano; R^4 is selected from the group consisting of hydrogen and iodo; R^5 is selected from the group consisting of $-\text{OH}$, and $-\text{OC}(\text{O})\text{R}^e$; R^3 is selected from the group consisting of
 30 iodo, bromo, optionally substituted $\text{C}_1\text{-C}_6$ alkyl, optionally substituted $-\text{CH}_2\text{aryl}$, optionally substituted $-\text{CH}(\text{OH})\text{aryl}$, $-\text{C}(\text{O})\text{-amido}$, $-\text{S}(=\text{O})_2\text{-amido}$ wherein the amido group is selected from the group consisting of phenethylamino, piperidinyl, 4-methylpiperizinyl, morpholinyl, cyclohexylamino, anilinyl, and indolinyl, and $-\text{SO}_2\text{R}^e$ wherein R^e is selected from the group consisting of phenyl, 4-chlorophenyl,

4-fluorophenyl, and 4-pyridyl; and R^7 is selected from the group consisting of hydrogen and fluoro.

172. The compound of claim 171 wherein G is -O-; R^1 and R^2 are each chloro; R^4 is hydrogen; R^7 is fluoro; R^5 is -OH; and R^3 is *i*-propyl.

5 173. The compound of claim 172 wherein X is selected from the group consisting of -PO₃H₂, -P(O)[-OCH₂OC(O)-*t*-butyl]₂, -P(O)[-OCH₂OC(O)O-*i*-propyl]₂, -P(O)[-N(H)CH(CH₃)C(O)OCH₂CH₃]₂, -P(O)[-N(H)C(CH₃)₂C(O)OCH₂CH₃]₂, -P(O)[-N(H)CH(CH₃)C(O)OCH₂CH₃][3,4-methylenedioxyphenyl], -P(O)[-N(H)C(CH₃)₂C(O)OCH₂CH₃][3,4-methylenedioxyphenyl],
10 and -P(O)[-OCH(3-chlorophenyl)CH₂CH₂O-].

174. The compound of claim 161 wherein T is -CH₂CH₂-; R^1 and R^2 are each independently selected from the group consisting of iodo, bromo, chloro, methyl, and cyano; R^4 is selected from the group consisting of hydrogen and iodo; R^5 is selected from the group consisting of -OH and -OC(O) R^e ; R^3 is selected from the group consisting of
15 iodo, bromo, optionally substituted C₁-C₆ alkyl, optionally substituted -CH₂aryl, optionally substituted -CH(OH)aryl, -C(O)-amido, -S(=O)₂-amido, wherein the amido group is selected from the group consisting of phenethylamino, piperidinyl, 4-methylpiperiziny, morpholinyl, cyclohexylamino, aniliny, and indolinyl, and -SO₂ R^e wherein R^e is selected from the group consisting of phenyl, 4-chlorophenyl,
20 4-fluorophenyl, and 4-pyridyl; and R^7 is selected from the group consisting of hydrogen and fluoro.

175. The compound of claim 174 wherein G is -O-; R^1 and R^2 are each chloro; R^4 is hydrogen; R^7 is fluoro; R^5 is -OH; and R^3 is *iso*-propyl.

176. The compound of claim 175 wherein X is selected from the group
25 consisting of -PO₃H₂, -P(O)[-OCH₂OC(O)-*t*-butyl]₂, -P(O)[-OCH₂OC(O)O-*i*-propyl]₂, -P(O)[-N(H)CH(CH₃)C(O)OCH₂CH₃]₂, -P(O)[-N(H)C(CH₃)₂C(O)OCH₂CH₃]₂, -P(O)[-N(H)CH(CH₃)C(O)OCH₂CH₃][3,4-methylenedioxyphenyl], -P(O)[-N(H)C(CH₃)₂C(O)OCH₂CH₃][3,4-methylenedioxyphenyl], and -P(O)[-OCH(3-chlorophenyl)CH₂CH₂O-].

177. The compound of claim 161 wherein T is -NHCH₂-; R^1 and R^2 are each independently selected from the group consisting of iodo, bromo, chloro, methyl, and cyano; R^4 is selected from the group consisting of hydrogen and iodo; R^5 is selected from the group consisting of -OH, and -OC(O) R^e ; R^3 is selected from the group consisting of
30 iodo, bromo, optionally substituted C₁-C₆ alkyl, optionally substituted -CH₂aryl,

optionally substituted -CH(OH)aryl, -C(O)-amido, -S(=O)₂-amido, wherein the amido group is selected from the group consisting of phenethylamino, piperidinyl, 4-methylpiperiziny, morpholinyl, cyclohexylamino, aniliny, and indoliny, and -SO₂R^e wherein R^e is selected from the group consisting of phenyl, 4-chlorophenyl, 4-fluorophenyl, and 4-pyridyl; and R⁷ is selected from the group consisting of hydrogen and fluoro.

178. The compound of claim 177 wherein G is -O-; R¹ and R² are each chloro; R⁷ is fluoro; R⁵ is -OH; and R³ is *iso*-propyl, then R⁴ is not hydrogen.

179. The compound of claim 177 wherein G is -O-; R¹ and R² are each bromo; R⁴ is hydrogen; R⁷ is fluoro; R⁵ is -OH; and R³ is *iso*-propyl.

180. The compound of claim 179 wherein X is selected from the group consisting of -PO₃H₂, -P(O)[-OCH₂OC(O)-*t*-butyl]₂, -P(O)[-OCH₂OC(O)O-*i*-propyl]₂, -P(O)[-N(H)CH(CH₃)C(O)OCH₂CH₃]₂, -P(O)[-N(H)C(CH₃)₂C(O)OCH₂CH₃]₂, -P(O)[-N(H)CH(CH₃)C(O)OCH₂CH₃][3,4-methylenedioxyphenyl], -P(O)[-N(H)C(CH₃)₂C(O)OCH₂CH₃][3,4-methylenedioxyphenyl], and -P(O)[-OCH(3-chlorophenyl)CH₂CH₂O-].

181. The compound of claim 163 wherein T is -N(H)C(O)-; R¹ and R² are each independently selected from the group consisting of iodo, bromo, chloro, methyl, and cyano; R⁴ is selected from the group consisting of hydrogen and iodo; R⁵ is selected from the group consisting of -OH and -OC(O)R^e; R³ is selected from the group consisting of iodo, bromo, optionally substituted -C₁-C₆ alkyl, optionally substituted -CH₂aryl, optionally substituted -CH(OH)aryl, -C(O)-amido, -S(=O)₂-amido, wherein the amido group is selected from the group consisting of phenethylamino, piperidinyl, 4-methylpiperiziny, morpholinyl, cyclohexylamino, aniliny, and indoliny, and -SO₂R^e wherein R^e is selected from the group consisting of phenyl, 4-chlorophenyl, 4-fluorophenyl, and 4-pyridyl; and R⁷ is selected from the group consisting of hydrogen and fluoro.

182. The compound of claim 181 wherein G is -O-; R¹ and R² are each chloro; R⁷ is fluoro; R⁴ is hydrogen; R⁵ is -OH; and R³ is *iso*-propyl.

183. The compound of claim 181 wherein X is selected from the group consisting of -PO₃H₂, -P(O)[-OCH₂OC(O)-*t*-butyl]₂, -P(O)[-OCH₂OC(O)O-*i*-propyl]₂, -P(O)[-N(H)CH(CH₃)C(O)OCH₂CH₃]₂, -P(O)[-N(H)C(CH₃)₂C(O)OCH₂CH₃]₂, -P(O)[-N(H)CH(CH₃)C(O)OCH₂CH₃][3,4-methylenedioxyphenyl],

-P(O)[-N(H)C(CH₃)₂C(O)OCH₂CH₃][3,4-methylenedioxyphenyl],
and -P(O)[-OCH(3-chlorophenyl)CH₂CH₂O-].

184. The compound of claim 163 wherein T is -OCH₂-; R¹ and R² are each independently selected from the group consisting of iodo, bromo, chloro, methyl, and cyano; R⁴ is selected from the group consisting of hydrogen and iodo; R⁵ is selected from the group consisting of -OH and -OC(O)R^e; R³ is selected from the group consisting of iodo, bromo, optionally substituted C₁-C₆ alkyl, optionally substituted -CH₂aryl, optionally substituted -CH(OH)aryl, -C(O)-amido, -S(=O)₂-amido, wherein the amido group is selected from the group consisting of phenethylamino, piperidinyl, 4-methylpiperizinyl, morpholinyl, cyclohexylamino, anilinyl, and indolinyl, and -SO₂R^e wherein R^e is selected from the group consisting of phenyl, 4-chlorophenyl, 4-fluorophenyl, and 4-pyridyl; and R⁷ is selected from the group consisting of hydrogen and fluoro.

185. The compound of claim 184 wherein G is -O-; R¹ and R² are each chloro; R⁴ is hydrogen; R⁷ is fluoro; R⁵ is -OH; and R³ is *iso*-propyl.

186. The compound of claim 184 wherein X is selected from the group consisting of -PO₃H₂, -P(O)[-OCH₂OC(O)-*t*-butyl]₂, -P(O)[-OCH₂OC(O)O-*i*-propyl]₂, -P(O)[-N(H)CH(CH₃)C(O)OCH₂CH₃]₂, -P(O)[-N(H)C(CH₃)₂C(O)OCH₂CH₃]₂, -P(O)[-N(H)CH(CH₃)C(O)OCH₂CH₃][3,4-methylenedioxyphenyl], -P(O)[-N(H)C(CH₃)₂C(O)OCH₂CH₃][3,4-methylenedioxyphenyl], and -P(O)[-OCH(3-chlorophenyl)CH₂CH₂O-].

187. The compound of claim 163 wherein T is -CH₂-; R¹ and R² are each independently selected from the group consisting of iodo, bromo, chloro, methyl, and cyano; R⁴ is selected from the group consisting of hydrogen and iodo; R⁵ is selected from the group consisting of -OH and -OC(O)R^e; R³ is selected from the group consisting of iodo, bromo, optionally substituted C₁-C₆ alkyl, optionally substituted -CH₂aryl, optionally substituted -CH(OH)aryl, -C(O)-amido, -S(=O)₂-amido, wherein the amido group is selected from the group consisting of phenethylamino, piperidinyl, 4-methylpiperizinyl, morpholinyl, cyclohexylamino, anilinyl, and indolinyl, and -SO₂R^e wherein R^e is selected from the group consisting of phenyl, 4-chlorophenyl, 4-fluorophenyl, and 4-pyridyl; and R⁷ is selected from the group consisting of hydrogen and fluoro.

188. The compound of claim 187 wherein G is -O-; R¹ and R² are each chloro; R⁷ is fluoro; R⁴ is hydrogen; R⁵ is -OH; and R³ is *i*-propyl.

189. The compound of claim 187 wherein X is selected from the group consisting of -PO₃H₂, -P(O)[-OCH₂OC(O)-*t*-butyl]₂, -P(O)[-OCH₂OC(O)O-*i*-propyl]₂,
 5 -P(O)[-N(H)CH(CH₃)C(O)OCH₂CH₃]₂, -P(O)[-N(H)C(CH₃)₂C(O)OCH₂CH₃]₂,
 -P(O)[-N(H)CH(CH₃)C(O)OCH₂CH₃][3,4-methylenedioxyphenyl],
 -P(O)[-N(H)C(CH₃)₂C(O)OCH₂CH₃][3,4-methylenedioxyphenyl],
 and -P(O)[-OCH(3-chlorophenyl)CH₂CH₂O-].

190. The compound of claim 163 wherein T is -CH₂CH₂-; R¹ and R² are each
 10 independently selected from the group consisting of iodo, bromo, chloro, methyl, and
 cyano; R⁴ is selected from the group consisting of hydrogen and iodo; R⁵ is selected from
 the group consisting of -OH and -OC(O)R^e; R³ is selected from the group consisting of
 iodo, bromo, optionally substituted C₁-C₆ alkyl, optionally substituted -CH₂aryl,
 optionally substituted -CH(OH)aryl, -C(O)-amido, -S(=O)₂-amido, wherein the amido
 15 group is selected from the group consisting of phenethylamino, piperidinyl,
 4-methylpiperizinyl, morpholinyl, cyclohexylamino, anilinyl, and indolinyl, wherein the
 amido group is selected from the group consisting of phenethylamino, piperidinyl,
 4-methylpiperizinyl, morpholinyl, cyclohexylamino, anilinyl, and indolinyl, and -SO₂R^e
 wherein R^e is selected from the group consisting of phenyl, 4-chlorophenyl,
 20 4-fluorophenyl, and 4-pyridyl; and R⁷ is selected from the group consisting of hydrogen
 and fluoro.

191. The compound of claim 190 wherein G is -O-; T is -CH₂CH₂-; R¹ and R²
 are each chloro; R⁴ is hydrogen; R⁷ is fluoro; R⁵ is -OH; and R³ is *iso*-propyl.

192. The compound of claim 190 wherein X is selected from the group
 25 consisting of -PO₃H₂, -P(O)[-OCH₂OC(O)-*t*-butyl]₂, -P(O)[-OCH₂OC(O)O-*i*-propyl]₂,
 -P(O)[-N(H)CH(CH₃)C(O)OCH₂CH₃]₂, -P(O)[-N(H)C(CH₃)₂C(O)OCH₂CH₃]₂,
 -P(O)[-N(H)CH(CH₃)C(O)OCH₂CH₃][3,4-methylenedioxyphenyl],
 -P(O)[-N(H)C(CH₃)₂C(O)OCH₂CH₃][3,4-methylenedioxyphenyl],
 and -P(O)[-OCH(3-chlorophenyl)CH₂CH₂O-].

193. The compound of claim 163 wherein T is -NHCH₂-; R¹ and R² are each
 30 independently selected from the group consisting of iodo, bromo, chloro, methyl, and
 cyano; R⁴ is selected from the group consisting of hydrogen and iodo; R⁵ is selected from
 the group consisting of -OH and -OC(O)R^e; R³ is selected from the group consisting of
 iodo, bromo, optionally substituted C₁-C₆ alkyl, optionally substituted -CH₂aryl,

optionally substituted -CH(OH)aryl, -C(O)-amido, -S(=O)₂-amido, wherein the amido group is selected from the group consisting of phenethylamino, piperidinyl, 4-methylpiperiziny, morpholinyl, cyclohexylamino, aniliny, and indolinyl, and -SO₂R^e wherein R^e is selected from the group consisting of phenyl, 4-chlorophenyl, 4-fluorophenyl, and 4-pyridyl; and R⁷ is selected from the group consisting of hydrogen and fluoro.

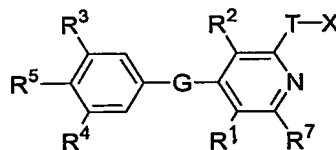
194. The compound of claim 193 wherein G is -O-; R¹ and R² are each chloro; R⁷ is fluoro; R⁵ is -OH; and R³ is *iso*-propyl, then R⁴ is not hydrogen

195. The compound of claim 193 wherein G is -O-; R¹ and R² are each bromo; R⁴ is hydrogen; R⁷ is fluoro; R⁵ is -OH; and R³ is *iso*-propyl.

196. The compound of claim 195 wherein X is selected from the group consisting of -PO₃H₂, -P(O)[-OCH₂OC(O)-*t*-butyl]₂, -P(O)[-OCH₂OC(O)O-*i*-propyl]₂, -P(O)[-N(H)CH(CH₃)C(O)OCH₂CH₃]₂, -P(O)[-N(H)C(CH₃)₂C(O)OCH₂CH₃]₂, -P(O)[-N(H)CH(CH₃)C(O)OCH₂CH₃][3,4-methylenedioxyphenyl], -P(O)[-N(H)C(CH₃)₂C(O)OCH₂CH₃][3,4-methylenedioxyphenyl], and -P(O)[-OCH(3-chlorophenyl)CH₂CH₂O-].

197. The compound as in any of claims 139, 140, 141, 142, 161, 163, 165, 167, 168, 170, 171, 173, 174, 176, 177, 180, 181, 183, 184, 186, 187, 189, 190, or 193, wherein X is -PO₃H₂.

198. The method of claim 83 wherein said phosphonic acid-containing compound is a compound of Formula III:



wherein:

G is selected from the group consisting of -O-, -S-, -S(=O)-, -S(=O)₂-, -CH₂-, -CF₂-, -CHF-, -C(O)-, -CH(OH)-, -NH-, and -N(C₁-C₄ alkyl)-;

T is selected from the group consisting of -(CR^a)_k-, -CR^b=CR^b-(CR^a)_n-, -(CR^a)_n-CR^b=CR^b-, -(CR^a)₂-CR^b=CR^b-(CR^a)₂-, -O(CR^b)₂(CR^a)_n-, -S(CR^b)₂(CR^a)_n-, -N(R^c)(CR^b)₂(CR^a)_n-, -N(R^b)C(O)(CR^a)_n-, -(CR^a)_nCH(NR^bR^c)-, -C(O)(CR^a)_m-, -(CR^a)_mC(O)-, -(CR^a)₂C(O)(CR^a)_n-, -(CR^a)₂C(O)(CR^a)₂-, and -C(O)NH(CR^b)₂(CR^a)_p-;

k is an integer from 0-4;

m is an integer from 0-3;

n is an integer from 0-2;

p is an integer from 0-1;

- 5 Each R^a is independently selected from the group consisting of hydrogen, optionally substituted $-C_1-C_4$ alkyl, halogen, $-OH$, optionally substituted $-O-C_1-C_4$ alkyl, $-OCF_3$, optionally substituted $-S-C_1-C_4$ alkyl, $-NR^bR^c$, optionally substituted $-C_2-C_4$ alkenyl, and optionally substituted $-C_2-C_4$ alkynyl; with the proviso that when one R^a is attached to C through an O, S, or N atom, then the other R^a attached
- 10 to the same C is a hydrogen, or attached via a carbon atom;

Each R^b is independently selected from the group consisting of hydrogen and optionally substituted $-C_1-C_4$ alkyl;

- Each R^c is independently selected from the group consisting of hydrogen and optionally substituted $-C_1-C_4$ alkyl, optionally substituted $-C(O)-C_1-C_4$ alkyl,
- 15 and $-C(O)H$;

R^1 and R^2 are each independently selected from the group consisting of halogen, optionally substituted $-C_1-C_4$ alkyl, optionally substituted $-S-C_1-C_3$ alkyl, optionally substituted $-C_2-C_4$ alkenyl, optionally substituted $-C_2-C_4$ alkynyl, $-CF_3$, $-OCF_3$, optionally substituted $-O-C_1-C_3$ alkyl, and cyano;

- 20 R^3 and R^4 are each independently selected from the group consisting of hydrogen, halogen, $-CF_3$, $-OCF_3$, cyano, optionally substituted $-C_1-C_{12}$ alkyl, optionally substituted $-C_2-C_{12}$ alkenyl, optionally substituted $-C_2-C_{12}$ alkynyl, optionally substituted $-(CR^a_2)_m$ aryl, optionally substituted $-(CR^a_2)_m$ cycloalkyl, optionally substituted $-(CR^a_2)_m$ heterocycloalkyl, $-OR^d$, $-SR^d$, $-S(=O)R^e$, $-S(=O)_2R^e$, $-S(=O)_2NR^fR^g$,
- 25 $-C(O)NR^fR^g$, $-C(O)OR^h$, $-C(O)R^e$, $-N(R^b)C(O)R^e$, $-N(R^b)C(O)NR^fR^g$, $-N(R^b)S(=O)_2R^e$, $-N(R^b)S(=O)_2NR^fR^g$, and $-NR^fR^g$;

- Each R^d is selected from the group consisting of optionally substituted $-C_1-C_{12}$ alkyl, optionally substituted $-C_2-C_{12}$ alkenyl, optionally substituted $-C_2-C_{12}$ alkynyl, optionally substituted $-(CR^b_2)_n$ aryl, optionally substituted $-(CR^b_2)_n$ cycloalkyl, optionally substituted $-(CR^b_2)_n$ heterocycloalkyl, and $-C(O)NR^fR^g$;
- 30

Each R^e is selected from the group consisting of optionally substituted $-C_1-C_{12}$ alkyl, optionally substituted $-C_2-C_{12}$ alkenyl, optionally substituted $-C_2-C_{12}$ alkynyl, optionally substituted $-(CR^a_2)_n$ aryl, optionally substituted $-(CR^a_2)_n$ cycloalkyl, and optionally substituted $-(CR^a_2)_n$ heterocycloalkyl;

R^f and R^g are each independently selected from the group consisting of hydrogen, optionally substituted $-C_1-C_{12}$ alkyl, optionally substituted $-C_2-C_{12}$ alkenyl, optionally substituted $-C_2-C_{12}$ alkynyl, optionally substituted $-(CR^b_2)_n$ aryl, optionally substituted $-(CR^b_2)_n$ cycloalkyl, and optionally substituted $-(CR^b_2)_n$ heterocycloalkyl, or R^f and R^g may together form an optionally substituted heterocyclic ring, which may contain a second heterogroup selected from the group consisting of O, NR^c , and S, wherein said optionally substituted heterocyclic ring may be substituted with 0-4 substituents selected from the group consisting of optionally substituted $-C_1-C_4$ alkyl, $-OR^b$, oxo, cyano, $-CF_3$, optionally substituted phenyl, and $-C(O)OR^h$;

Each R^h is selected from the group consisting of optionally substituted $-C_1-C_{12}$ alkyl, optionally substituted $-C_2-C_{12}$ alkenyl, optionally substituted $-C_2-C_{12}$ alkynyl, optionally substituted $-(CR^b_2)_n$ aryl, optionally substituted $-(CR^b_2)_n$ cycloalkyl, and optionally substituted $-(CR^b_2)_n$ heterocycloalkyl;

R^5 is selected from the group consisting of $-OH$, optionally substituted $-OC_1-C_6$ alkyl, $-OC(O)R^e$, $-OC(O)OR^h$, $-F$, $-NHC(O)R^e$, $-NHS(=O)R^e$, $-NHS(=O)_2R^e$, $-NHC(=S)NH(R^h)$, and $-NHC(O)NH(R^h)$;

R^7 is selected from the group consisting of hydrogen, halogen, amino, hydroxyl, $-O-C_1-C_4$ alkyl, $-SH$ and $-S-C_1-C_4$ alkyl;

X is $P(O)YR^{11}Y'R^{11}$;

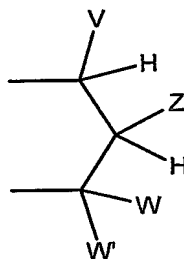
Y and Y' are each independently selected from the group consisting of $-O-$, and $-NR^v-$; when Y and Y' are $-O-$, R^{11} attached to $-O-$ is independently selected from the group consisting of $-H$, alkyl, optionally substituted aryl, optionally substituted heterocycloalkyl, optionally substituted CH_2 -heterocycloalkyl wherein the cyclic moiety contains a carbonate or thiocarbonate, optionally substituted $-alkylaryl$, $-C(R^z)_2OC(O)NR^z_2$, $-NR^z-C(O)-R^y$, $-C(R^z)_2-OC(O)R^y$, $-C(R^z)_2-O-C(O)OR^y$, $-C(R^z)_2OC(O)SR^y$, $-alkyl-S-C(O)R^y$, $-alkyl-S-S-alkylhydroxy$, and $-alkyl-S-S-S-alkylhydroxy$;

when Y and Y' are $-NR^v-$, then R^{11} attached to $-NR^v-$ is independently selected from the group consisting of $-H$, $-[C(R^z)_2]_q-COOR^y$, $-C(R^x)_2COOR^y$, $-[C(R^z)_2]_q-C(O)SR^y$, and $-cycloalkylene-COOR^y$;

when Y is $-O-$ and Y' is NR^v , then R^{11} attached to $-O-$ is independently selected from the group consisting of $-H$, alkyl, optionally substituted aryl, optionally substituted heterocycloalkyl, optionally substituted CH_2 -heterocycloalkyl wherein the cyclic moiety

contains a carbonate or thiocarbonate, optionally substituted -alkylaryl,
 $-C(R^Z)_2OC(O)NR^Z$, $-NR^Z-C(O)-R^Y$, $-C(R^Z)_2-OC(O)R^Y$,
 $-C(R^Z)_2-O-C(O)OR^Y$, $-C(R^Z)_2OC(O)SR^Y$, -alkyl-S-C(O) R^Y , -alkyl-S-S-alkylhydroxy,
 and -alkyl-S-S-S-alkylhydroxy; and R^{11} attached to $-NR^V-$ is independently selected from
 5 the group consisting of -H, $-[C(R^Z)_2]_q-COOR^Y$, $-C(R^X)_2COOR^Y$, $-[C(R^Z)_2]_q-C(O)SR^Y$,
 and -cycloalkylene- $COOR^Y$;

or when Y and Y' are independently selected from -O- and $-NR^V-$, then together
 R^{11} and R^{11} are -alkyl-S-S-alkyl- to form a cyclic group, or together R^{11} and R^{11} are the
 group:



10

wherein:

V, W, and W' are independently selected from the group consisting of hydrogen,
 optionally substituted alkyl, optionally substituted aralkyl, heterocycloalkyl, aryl,
 substituted aryl, heteroaryl, substituted heteroaryl, optionally substituted 1-alkenyl, and
 15 optionally substituted 1-alkynyl;

or together V and Z are connected via an additional 3-5 atoms to form a cyclic
 group containing 5-7 atoms, wherein 0-1 atoms are heteroatoms and the remaining
 atoms are carbon, substituted with hydroxy, acyloxy, alkylthiocarbonyloxy,
 alkoxy carbonyloxy, or aryloxy carbonyloxy attached to a carbon atom that is three atoms
 20 from both Y groups attached to the phosphorus; or

or together V and Z are connected via an additional 3-5 atoms to form a cyclic
 group, wherein 0-1 atoms are heteroatoms and the remaining atoms are carbon, that is
 fused to an aryl group at the beta and gamma position to the Y attached to the
 phosphorus;

25 or together V and W are connected via an additional 3 carbon atoms to form an
 optionally substituted cyclic group containing 6 carbon atoms and substituted with one
 substituent selected from the group consisting of hydroxy, acyloxy, alkoxy carbonyloxy,

alkylthiocarbonyloxy, and aryloxy carbonyloxy, attached to one of said carbon atoms that is three atoms from a Y attached to the phosphorus;

or together Z and W are connected via an additional 3-5 atoms to form a cyclic group, wherein 0-1 atoms are heteroatoms and the remaining atoms are carbon, and V
5 must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

or together W and W' are connected via an additional 2-5 atoms to form a cyclic group, wherein 0-2 atoms are heteroatoms and the remaining atoms are carbon, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

Z is selected from the group consisting of -CHR^zOH, -CHR^zOC(O)R^y,
10 -CHR^zOC(S)R^y, -CHR^zOC(S)OR^y, -CHR^zOC(O)SR^y, -CHR^zOCO₂R^y, -OR^z,
-SR^z, -CHR^zN₃, -CH₂aryl, -CH(aryl)OH, -CH(CH=CR^z)OH, -CH(C≡CR^z)OH,
-R^z, -NR^z₂, -OCOR^y, -OCO₂R^y, -SCOR^y, -SCO₂R^y, -NHCOR^z, -NHCO₂R^y, -CH₂NHaryl,
-(CH₂)_q-OR^z, and -(CH₂)_q-SR^z;

q is an integer 2 or 3;

15 Each R^z is selected from the group consisting of R^y and -H;

Each R^y is selected from the group consisting of alkyl, aryl, heterocycloalkyl, and aralkyl;

Each R^x is independently selected from the group consisting of -H, and alkyl, or together R^x and R^x form a cyclic alkyl group;

20 Each R^v is selected from the group consisting of -H, lower alkyl, acyloxyalkyl, alkoxy carbonyloxyalkyl, and lower acyl;

with the provisos that:

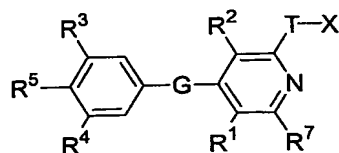
a) when G is -O-, T is -NH-CH₂-, R¹ and R² are each chloro, R³ is *iso*-propyl, R⁴ is hydrogen, R⁷ is fluoro, and R⁵ is -OH, then X is not P(O)(OH)₂,
25 P(O)(OH)(OCH₃) or P(O)(OCH₃)₂;

b) V, Z, W, W' are not all -H; and

c) when Z is -R^z, then at least one of V, W, and W' is not -H, alkyl, aralkyl, or heterocycloalkyl;

and pharmaceutically acceptable salts and prodrugs thereof and pharmaceutically
30 acceptable salts of said prodrugs.

199. The method of claim 83 wherein said phosphonic acid-containing compound is a compound of Formula III:



wherein:

G is selected from the group consisting of -O-, -S-, -S(=O)-, -S(=O)₂-,
-CH₂-, -CF₂-, -CHF-, -C(O)-, -CH(OH)-, -NH-, and -N(C₁-C₄ alkyl)-;

5 T is selected from the group consisting of -(CR^a₂)_k-, -CR^b=CR^b-(CR^a₂)_n-,
-(CR^a₂)_n-CR^b=CR^b-, -(CR^a₂)-CR^b=CR^b-(CR^a₂)-,
-O(CR^b₂)(CR^a₂)_n-, -S(CR^b₂)(CR^a₂)_n-, -N(R^c)(CR^b₂)(CR^a₂)_n-, -N(R^b)C(O)(CR^a₂)_n-,
-(CR^a₂)_nCH(NR^bR^c)-, -C(O)(CR^a₂)_m-, -(CR^a₂)_mC(O)-, -(CR^a₂)C(O)(CR^a₂)_n-,
-(CR^a₂)_nC(O)(CR^a₂)-, and -C(O)NH(CR^b₂)(CR^a₂)_p-;

10 k is an integer from 0-4;

m is an integer from 0-3;

n is an integer from 0-2;

p is an integer from 0-1;

Each R^a is independently selected from the group consisting of hydrogen,
15 optionally substituted -C₁-C₄ alkyl, halogen, -OH, optionally substituted -O-C₁-C₄
alkyl, -OCF₃, optionally substituted -S-C₁-C₄ alkyl, -NR^bR^c, optionally
substituted -C₂-C₄ alkenyl, and optionally substituted -C₂-C₄ alkynyl; with the proviso
that when one R^a is attached to C through an O, S, or N atom, then the other R^a attached
to the same C is a hydrogen, or attached via a carbon atom;

20 Each R^b is independently selected from the group consisting of hydrogen and
optionally substituted -C₁-C₄ alkyl;

Each R^c is independently selected from the group consisting of hydrogen,
optionally substituted -C₁-C₄ alkyl, optionally substituted -C(O)-C₁-C₄ alkyl,
and -C(O)H;

25 R¹ and R² are each independently selected from the group consisting of halogen,
optionally substituted -C₁-C₄ alkyl, optionally substituted -S-C₁-C₃ alkyl, optionally
substituted -C₂-C₄ alkenyl, optionally substituted -C₂-C₄ alkynyl, -CF₃, -OCF₃, optionally
substituted -O-C₁-C₃ alkyl, and cyano;

R³ and R⁴ are each independently selected from the group consisting of hydrogen,
30 halogen, -CF₃, -OCF₃, cyano, optionally substituted -C₁-C₁₂ alkyl, optionally
substituted -C₂-C₁₂ alkenyl, optionally substituted -C₂-C₁₂ alkynyl, optionally

substituted $-(CR^a)_m$ aryl, optionally substituted $-(CR^a)_m$ cycloalkyl, optionally substituted $(CR^a)_m$ heterocycloalkyl, $-OR^d$, $-SR^d$, $-S(=O)R^e$, $-S(=O)_2R^e$, $-S(=O)_2NR^fR^g$, $-C(O)NR^fR^g$, $-C(O)OR^h$, $-C(O)R^e$, $-N(R^b)C(O)R^e$, $-N(R^b)C(O)NR^fR^g$, $-N(R^b)S(=O)_2R^e$, $-N(R^b)S(=O)_2NR^fR^g$, and $-NR^fR^g$;

- 5 Each R^d is selected from the group consisting of optionally substituted $-C_1$ - C_{12} alkyl, optionally substituted $-C_2$ - C_{12} alkenyl, optionally substituted $-C_2$ - C_{12} alkynyl, optionally substituted $-(CR^b)_n$ aryl, optionally substituted $-(CR^b)_n$ cycloalkyl, optionally substituted $-(CR^b)_n$ heterocycloalkyl, and $-C(O)NR^fR^g$;

- Each R^e is optionally substituted $-C_1$ - C_{12} alkyl, optionally substituted $-C_2$ - C_{12} alkenyl, optionally substituted $-C_2$ - C_{12} alkynyl, optionally substituted $-(CR^a)_n$ aryl, optionally substituted $-(CR^a)_n$ cycloalkyl, and optionally substituted $-(CR^a)_n$ heterocycloalkyl;
- 10

- R^f and R^g are each independently selected from the group consisting of hydrogen, optionally substituted $-C_1$ - C_{12} alkyl, optionally substituted $-C_2$ - C_{12} alkenyl, optionally substituted $-C_2$ - C_{12} alkynyl, optionally substituted $-(CR^b)_n$ aryl, optionally substituted $-(CR^b)_n$ cycloalkyl, and optionally substituted $-(CR^b)_n$ heterocycloalkyl, or R^f and R^g may together form an optionally substituted heterocyclic ring, which may contain a second heterogroup selected from the group of O, NR^c , and S, wherein said optionally substituted heterocyclic ring may be substituted with 0-4 substituents selected from the group consisting of optionally substituted $-C_1$ - C_4 alkyl, $-OR^b$, oxo, cyano, $-CF_3$, optionally substituted phenyl, and $-C(O)OR^h$;
- 15
- 20

- Each R^h is selected from the group consisting of optionally substituted $-C_1$ - C_{12} alkyl, optionally substituted $-C_2$ - C_{12} alkenyl, optionally substituted $-C_2$ - C_{12} alkynyl, optionally substituted $-(CR^b)_n$ aryl, optionally substituted $-(CR^b)_n$ cycloalkyl, and optionally substituted $-(CR^b)_n$ heterocycloalkyl;
- 25

R^5 is selected from the group consisting of $-OH$, optionally substituted $-OC_1$ - C_6 alkyl, $-OC(O)R^e$, $-OC(O)OR^h$, $-F$, $-NHC(O)R^e$, $-NHS(=O)_2R^e$, $-NHS(=O)R^e$, $-NHC(=S)NH(R^h)$, and $-NHC(O)NH(R^h)$;

- R^7 is selected from the group consisting of hydrogen, halogen, amino, hydroxyl, $-O$ - C_1 - C_4 alkyl, $-SH$ and $-S$ - C_1 - C_4 alkyl;
- 30

X is $P(O)YR^{11}Y'R^{11}$;

Y and Y' are each independently selected from the group consisting of $-O$ -, and $-NR^v$ -; when Y and Y' are $-O$ -, R^{11} attached to $-O$ - is independently selected from the group consisting of $-H$, alkyl, optionally substituted aryl, optionally substituted

heterocycloalkyl, optionally substituted CH_2 -heterocycloalkyl wherein the cyclic moiety contains a carbonate or thiocarbonate, optionally substituted -alkylaryl,

$-\text{C}(\text{R}^z)_2\text{OC}(\text{O})\text{NR}^z$, $-\text{NR}^z-\text{C}(\text{O})-\text{R}^y$, $-\text{C}(\text{R}^z)_2-\text{OC}(\text{O})\text{R}^y$,

$-\text{C}(\text{R}^z)_2-\text{O}-\text{C}(\text{O})\text{OR}^y$, $-\text{C}(\text{R}^z)_2\text{OC}(\text{O})\text{SR}^y$, -alkyl-S-C(O) R^y , -alkyl-S-S-alkylhydroxy,

5 and -alkyl-S-S-S-alkylhydroxy;

when Y and Y' are $-\text{NR}^v$ -, then R^{11} attached to $-\text{NR}^v$ - is independently selected from the group consisting

of -H, $-\text{[C}(\text{R}^z)_2\text{]}_q-\text{COOR}^y$, $-\text{C}(\text{R}^x)_2\text{COOR}^y$, $-\text{[C}(\text{R}^z)_2\text{]}_q-\text{C}(\text{O})\text{SR}^y$,

and -cycloalkylene- COOR^y ;

10 when Y is -O- and Y' is NR^v , then R^{11} attached to -O- is independently selected from the group consisting of -H, alkyl, optionally substituted aryl, optionally substituted heterocycloalkyl, optionally substituted CH_2 -heterocycloalkyl wherein the cyclic moiety contains a carbonate or thiocarbonate, optionally

substituted -alkylaryl, $-\text{C}(\text{R}^z)_2\text{OC}(\text{O})\text{NR}^z$, $-\text{NR}^z-\text{C}(\text{O})-\text{R}^y$, $-\text{C}(\text{R}^z)_2-\text{OC}(\text{O})\text{R}^y$,

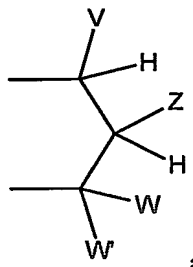
15 $-\text{C}(\text{R}^z)_2-\text{O}-\text{C}(\text{O})\text{OR}^y$, $-\text{C}(\text{R}^z)_2\text{OC}(\text{O})\text{SR}^y$, -alkyl-S-C(O) R^y , -alkyl-S-S-alkylhydroxy,

and -alkyl-S-S-S-alkylhydroxy; and R^{11} attached to $-\text{NR}^v$ - is independently selected from

the group consisting of -H, $-\text{[C}(\text{R}^z)_2\text{]}_q-\text{COOR}^y$, $-\text{C}(\text{R}^x)_2\text{COOR}^y$, $-\text{[C}(\text{R}^z)_2\text{]}_q-\text{C}(\text{O})\text{SR}^y$,

and -cycloalkylene- COOR^y ;

or when Y and Y' are independently selected from -O- and $-\text{NR}^v$ -, then together
20 R^{11} and R^{11} are -alkyl-S-S-alkyl- to form a cyclic group, or together R^{11} and R^{11} are the group:



wherein:

V, W, and W' are independently selected from the group consisting of hydrogen,
25 optionally substituted alkyl, optionally substituted aralkyl, heterocycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, optionally substituted 1-alkenyl, and optionally substituted 1-alkynyl;

or together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 atoms, wherein 0 – 1 atoms are heteroatoms and the remaining atoms are carbon, substituted with hydroxy, acyloxy, alkylthiocarbonyloxy, alkoxycarbonyloxy, or aryloxycarbonyloxy attached to a carbon atom that is three atoms
 5 from both Y groups attached to the phosphorus; or

or together V and Z are connected via an additional 3-5 atoms to form a cyclic group, wherein 0-1 atoms are heteroatoms and the remaining atoms are carbon, that is fused to an aryl group at the beta and gamma position to the Y attached to the phosphorus;

10 or together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to one of said carbon atoms that is three atoms from a Y attached to the phosphorus;

15 or together Z and W are connected via an additional 3-5 atoms to form a cyclic group, wherein 0-1 atoms are heteroatoms and the remaining atoms are carbon, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

or together W and W' are connected via an additional 2-5 atoms to form a cyclic group, wherein 0-2 atoms are heteroatoms and the remaining atoms are carbon, and V
 20 must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

Z is selected from the group consisting of $-\text{CHR}^z\text{OH}$, $-\text{CHR}^z\text{OC}(\text{O})\text{R}^y$, $-\text{CHR}^z\text{OC}(\text{S})\text{R}^y$, $-\text{CHR}^z\text{OC}(\text{S})\text{OR}^y$, $-\text{CHR}^z\text{OC}(\text{O})\text{SR}^y$, $-\text{CHR}^z\text{OCO}_2\text{R}^y$, $-\text{OR}^z$, $-\text{SR}^z$, $-\text{CHR}^z\text{N}_3$, $-\text{CH}_2\text{aryl}$, $-\text{CH}(\text{aryl})\text{OH}$, $-\text{CH}(\text{CH}=\text{CR}^z_2)\text{OH}$, $-\text{CH}(\text{C}\equiv\text{CR}^z_2)\text{OH}$, $-\text{R}^z$, $-\text{NR}^z_2$, $-\text{OCOR}^y$, $-\text{OCO}_2\text{R}^y$, $-\text{SCOR}^y$, $-\text{SCO}_2\text{R}^y$, $-\text{NHCOR}^z$, $-\text{NHCO}_2\text{R}^y$, $-\text{CH}_2\text{NHaryl}$,
 25 $-(\text{CH}_2)_q-\text{OR}^z$, and $-(\text{CH}_2)_q-\text{SR}^z$;

q is an integer 2 or 3;

Each R^z is selected from the group consisting of R^y and $-\text{H}$;

Each R^y is selected from the group consisting of alkyl, aryl, heterocycloalkyl, and aralkyl;

30 Each R^x is independently selected from the group consisting of $-\text{H}$, and alkyl, or together R^x and R^x form a cyclic alkyl group;

Each R^v is selected from the group consisting of $-\text{H}$, lower alkyl, acyloxyalkyl, alkoxycarbonyloxyalkyl, and lower acyl;

with the provisos that:

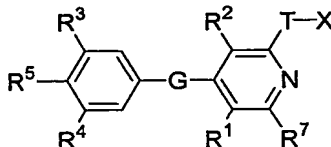
- a) when G is selected from the group consisting of -O-, -S-, -S(=O)-, -S(=O)₂-, -CH₂-, -C(O)- and -NR^b-; T is -A-B- where A is selected from the group consisting of -NR^b-, -O-, -CH₂- and -S- and B is selected from the group consisting of a bond and substituted or unsubstituted C₁-C₃ alkyl; R³ is selected from the group consisting of halogen, trifluoromethyl, substituted or unsubstituted C₁-C₆ alkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, aryloxy, substituted amide, sulfone, sulfonamide and C₃-C₇ cycloalkyl, wherein said aryl, heteroaryl or cycloalkyl ring(s) are attached or fused to the aromatic; R⁴ is selected from the group consisting of hydrogen, halogen, substituted or unsubstituted C₁-C₆ alkyl, substituted or unsubstituted aryl, and substituted or unsubstituted heteroaryl; R¹ and R² are each independently selected from the group consisting of halogen, substituted or unsubstituted C₁-C₄ alkyl, and substituted or unsubstituted C₃-C₅ cycloalkyl; R⁷ is selected from the group consisting of hydrogen, halogen, amino, hydroxyl, -O-C₁-C₄ alkyl, -SH and -S-C₁-C₄ alkyl; and R⁵ is selected from the group consisting of hydroxyl, optionally substituted -OC₁-C₆ alkyl, and -OC(O)R^e; then X is not -P(O)(OH)₂;
- b) V, Z, W, W' are not all -H; and
- c) when Z is -R^z, then at least one of V, W, and W' is not -H, alkyl, aralkyl, or heterocycloalkyl;
- and pharmaceutically acceptable salts and prodrugs thereof and pharmaceutically acceptable salts of said prodrugs.

200. The method of claim 198 wherein when G is -O-, T is -NH-CH₂-, R¹ and R² are each chloro, R³ is *iso*-propyl, R⁷ is fluoro, and R⁵ is -OH, then R⁴ is not hydrogen.

201. The method of claim 199 wherein when G is selected from the group consisting of -O-, -S-, -S(=O)-, -S(=O)₂-, -CH₂-, -C(O)- and -NR^b-; T is -A-B- where A is selected from the group consisting of -NR^b-, -O-, -CH₂- and -S- and B is selected from the group consisting of a bond and substituted or unsubstituted C₁-C₃ alkyl; R³ is selected from the group consisting of halogen, trifluoromethyl, substituted or unsubstituted C₁-C₆ alkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, aryloxy, substituted amide, sulfone, sulfonamide and C₃-C₇ cycloalkyl, wherein said aryl, heteroaryl or cycloalkyl ring(s) are attached or fused to the aromatic; R⁴ is selected from the group consisting of hydrogen, halogen, substituted or unsubstituted C₁-C₆ alkyl, substituted or unsubstituted aryl, and substituted or

unsubstituted heteroaryl; R^1 and R^2 are each independently selected from the group consisting of halogen, substituted or unsubstituted C_1 - C_4 alkyl, substituted or unsubstituted C_3 - C_5 cycloalkyl; and R^7 is selected from the group consisting of hydrogen, halogen, amino, hydroxyl, $-O$ - C_1 - C_4 alkyl, $-SH$ and $-S$ - C_1 - C_4 alkyl; then R^5 is not hydroxyl, optionally substituted $-OC_1$ - C_6 alkyl, or $-OC(O)R^e$.

202. The method of claim 100 wherein said phosphonic acid-containing compound is a compound of Formula III:



wherein:

10 G is selected from the group consisting of $-O-$, $-S-$, $-S(=O)-$, $-S(=O)_2-$, $-CH_2-$, $-CF_2-$, $-CHF-$, $-C(O)-$, $-CH(OH)-$, $-NH-$, and $-N(C_1-C_4 \text{ alkyl})-$;

T is selected from the group consisting of $-(CR^a_2)_k-$, $-CR^b=CR^b-(CR^a_2)_n-$, $-(CR^a_2)_n-CR^b=CR^b-$, $-(CR^a_2)-CR^b=CR^b-(CR^a_2)-$, $-O(CR^b_2)(CR^a_2)_n-$, $-S(CR^b_2)(CR^a_2)_n-$, $-N(R^c)(CR^b_2)(CR^a_2)_n-$, $-N(R^b)C(O)(CR^a_2)_n-$, $-(CR^a_2)_nCH(NR^bR^c)-$, $-C(O)(CR^a_2)_m-$, $-(CR^a_2)_mC(O)-$, $-(CR^a_2)C(O)(CR^a_2)_n-$, $-(CR^a_2)_nC(O)(CR^a_2)-$, and $-C(O)NH(CR^b_2)(CR^a_2)_p-$;

k is an integer from 0-4;

m is an integer from 0-3;

n is an integer from 0-2;

20 p is an integer from 0-1;

Each R^a is independently selected from the group consisting of hydrogen, optionally substituted $-C_1$ - C_4 alkyl, halogen, $-OH$, optionally substituted $-O$ - C_1 - C_4 alkyl, $-OCF_3$, optionally substituted $-S$ - C_1 - C_4 alkyl, $-NR^bR^c$, optionally substituted $-C_2$ - C_4 alkenyl, and optionally substituted $-C_2$ - C_4 alkynyl; with the proviso that when one R^a is attached to C through an O , S , or N atom, then the other R^a attached to the same C is a hydrogen, or attached via a carbon atom;

Each R^b is independently selected from the group consisting of hydrogen and optionally substituted $-C_1$ - C_4 alkyl;

Each R^c is independently selected from the group consisting of hydrogen and optionally substituted $-C_1-C_4$ alkyl, optionally substituted $-C(O)-C_1-C_4$ alkyl, and $-C(O)H$;

R^1 and R^2 are each independently selected from the group consisting of halogen, optionally substituted $-C_1-C_4$ alkyl, optionally substituted $-S-C_1-C_3$ alkyl, optionally substituted $-C_2-C_4$ alkenyl, optionally substituted $-C_2-C_4$ alkynyl, $-CF_3$, $-OCF_3$, optionally substituted $-O-C_1-C_3$ alkyl, and cyano;

R^3 and R^4 are each independently selected from the group consisting of hydrogen, halogen, $-CF_3$, $-OCF_3$, cyano, optionally substituted $-C_1-C_{12}$ alkyl, optionally substituted $-C_2-C_{12}$ alkenyl, optionally substituted $-C_2-C_{12}$ alkynyl, optionally substituted $-(CR^a)_m$ aryl, optionally substituted $-(CR^a)_m$ cycloalkyl, optionally substituted $-(CR^a)_m$ heterocycloalkyl, $-OR^d$, $-SR^d$, $-S(=O)R^e$, $-S(=O)_2R^e$, $-S(=O)_2NR^fR^g$, $-C(O)NR^fR^g$, $-C(O)OR^h$, $-C(O)R^e$, $-N(R^b)C(O)R^e$, $-N(R^b)C(O)NR^fR^g$, $-N(R^b)S(=O)_2R^e$, $-N(R^b)S(=O)_2NR^fR^g$, and $-NR^fR^g$;

Each R^d is selected from the group consisting of optionally substituted $-C_1-C_{12}$ alkyl, optionally substituted $-C_2-C_{12}$ alkenyl, optionally substituted $-C_2-C_{12}$ alkynyl, optionally substituted $-(CR^b)_n$ aryl, optionally substituted $-(CR^b)_n$ cycloalkyl, optionally substituted $-(CR^b)_n$ heterocycloalkyl, and $-C(O)NR^fR^g$;

Each R^e is selected from the group consisting of optionally substituted $-C_1-C_{12}$ alkyl, optionally substituted $-C_2-C_{12}$ alkenyl, optionally substituted $-C_2-C_{12}$ alkynyl, optionally substituted $-(CR^a)_n$ aryl, optionally substituted $-(CR^a)_n$ cycloalkyl, and optionally substituted $-(CR^a)_n$ heterocycloalkyl;

R^f and R^g are each independently selected from the group consisting of hydrogen, optionally substituted $-C_1-C_{12}$ alkyl, optionally substituted $-C_2-C_{12}$ alkenyl, optionally substituted $-C_2-C_{12}$ alkynyl, optionally substituted $-(CR^b)_n$ aryl, optionally substituted $-(CR^b)_n$ cycloalkyl, and optionally substituted $-(CR^b)_n$ heterocycloalkyl, or R^f and R^g may together form an optionally substituted heterocyclic ring, which may contain a second heterogroup selected from the group consisting of O, NR^c , and S, wherein said optionally substituted heterocyclic ring may be substituted with 0-4 substituents selected from the group consisting of optionally substituted $-C_1-C_4$ alkyl, $-OR^b$, oxo, cyano, $-CF_3$, optionally substituted phenyl, and $-C(O)OR^h$;

Each R^h is selected from the group consisting of optionally substituted $-C_1-C_{12}$ alkyl, optionally substituted $-C_2-C_{12}$ alkenyl, optionally substituted $-C_2-C_{12}$ alkynyl,

optionally substituted $-(CR^b)_n$ aryl, optionally substituted $-(CR^b)_n$ cycloalkyl, and optionally substituted $-(CR^b)_n$ heterocycloalkyl;

R^5 is selected from the group consisting of -OH, optionally substituted $-OC_1-C_6$ alkyl, $-OC(O)R^e$, $-OC(O)OR^h$, -F, $-NHC(O)R^e$, $-NHS(=O)R^e$, $-NHS(=O)_2R^e$,

5 $-NHC(=S)NH(R^h)$, and $-NHC(O)NH(R^h)$;

R^7 is selected from the group consisting of hydrogen, halogen, amino, hydroxyl, $-O-C_1-C_4$ alkyl, -SH and $-S-C_1-C_4$ alkyl;

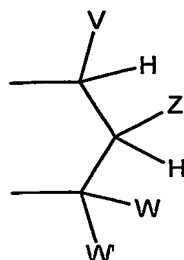
X is $P(O)YR^{11}Y'R^{11}$;

Y and Y' are each independently selected from the group consisting of -O-,
 10 and $-NR^v$ -; when Y and Y' are -O-, R^{11} attached to -O- is independently selected from the group consisting of -H, alkyl, optionally substituted aryl, optionally substituted heterocycloalkyl, optionally substituted CH_2 -heterocycloalkyl wherein the cyclic moiety contains a carbonate or thiocarbonate, optionally substituted -alkylaryl, $-C(R^z)_2OC(O)NR^z$, $-NR^z-C(O)-R^y$, $-C(R^z)_2-OC(O)R^y$,
 15 $-C(R^z)_2-O-C(O)OR^y$, $-C(R^z)_2OC(O)SR^y$, -alkyl-S-C(O) R^y , -alkyl-S-S-alkylhydroxy, and -alkyl-S-S-S-alkylhydroxy;

when Y and Y' are $-NR^v$ -, then R^{11} attached to $-NR^v$ - is independently selected from the group consisting of -H, $-[C(R^z)_2]_q-COOR^y$, $-C(R^x)_2COOR^y$, $-[C(R^z)_2]_q-C(O)SR^y$,
 20 and -cycloalkylene- $COOR^y$;

when Y is -O- and Y' is NR^v , then R^{11} attached to -O- is independently selected from the group consisting of -H, alkyl, optionally substituted aryl, optionally substituted heterocycloalkyl, optionally substituted CH_2 -heterocycloalkyl wherein the cyclic moiety contains a carbonate or thiocarbonate, optionally substituted -alkylaryl,
 25 $-C(R^z)_2OC(O)NR^z$, $-NR^z-C(O)-R^y$, $-C(R^z)_2-OC(O)R^y$, $-C(R^z)_2-O-C(O)OR^y$, $-C(R^z)_2OC(O)SR^y$, -alkyl-S-C(O) R^y , -alkyl-S-S-alkylhydroxy, and -alkyl-S-S-S-alkylhydroxy; and R^{11} attached to $-NR^v$ - is independently selected from the group consisting of -H, $-[C(R^z)_2]_q-COOR^y$, $-C(R^x)_2COOR^y$, $-[C(R^z)_2]_q-C(O)SR^y$, and -cycloalkylene- $COOR^y$;

30 or when Y and Y' are independently selected from -O- and $-NR^v$ -, then together R^{11} and R^{11} are -alkyl-S-S-alkyl- to form a cyclic group, or together R^{11} and R^{11} are the group:



wherein:

V, W, and W' are independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted aralkyl, heterocycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, optionally substituted 1-alkenyl, and optionally substituted 1-alkynyl;

or together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 atoms, wherein 0-1 atoms are heteroatoms and the remaining atoms are carbon, substituted with hydroxy, acyloxy, alkylthiocarbonyloxy, alkoxy, alkoxy, or aryloxy, attached to a carbon atom that is three atoms from both Y groups attached to the phosphorus; or

or together V and Z are connected via an additional 3-5 atoms to form a cyclic group, wherein 0-1 atoms are heteroatoms and the remaining atoms are carbon, that is fused to an aryl group at the beta and gamma position to the Y attached to the phosphorus;

or together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxy, alkoxy, alkylthiocarbonyloxy, and aryloxy, attached to one of said carbon atoms that is three atoms from a Y attached to the phosphorus;

or together Z and W are connected via an additional 3-5 atoms to form a cyclic group, wherein 0-1 atoms are heteroatoms and the remaining atoms are carbon, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

or together W and W' are connected via an additional 2-5 atoms to form a cyclic group, wherein 0-2 atoms are heteroatoms and the remaining atoms are carbon, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

Z is selected from the group consisting of $-\text{CHR}^z\text{OH}$, $-\text{CHR}^z\text{OC(O)R}^y$, $-\text{CHR}^z\text{OC(S)R}^y$, $-\text{CHR}^z\text{OC(S)OR}^y$, $-\text{CHR}^z\text{OC(O)SR}^y$, $-\text{CHR}^z\text{OCO}_2\text{R}^y$, $-\text{OR}^z$,

-SR^z, -CHR^zN₃, -CH₂aryl, -CH(aryl)OH, -CH(CH=CR^z)OH, -CH(C≡CR^z)OH, -R^z, -NR^z₂, -OCOR^y, -OCO₂R^y, -SCOR^y, -SCO₂R^y, -NHCOR^z, -NHCO₂R^y, -CH₂NHaryl, -(CH₂)_q-OR^z, and -(CH₂)_q-SR^z;

q is an integer 2 or 3;

5 Each R^z is selected from the group consisting of R^y and -H;

Each R^y is selected from the group consisting of alkyl, aryl, heterocycloalkyl, and aralkyl;

Each R^x is independently selected from the group consisting of -H, and alkyl, or together R^x and R^x form a cyclic alkyl group;

10 Each R^v is selected from the group consisting of -H, lower alkyl, acyloxyalkyl, alkoxy-carbonyloxyalkyl, and lower acyl;

with the provisos that:

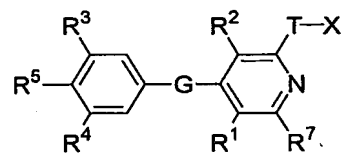
a) when G is -O-, T is -NH-CH₂-, R¹ and R² are each chloro, R³ is *iso*-propyl, R⁴ is hydrogen, R⁷ is fluoro and R⁵ is -OH, then X is not P(O)(OH)₂,
15 P(O)(OH)(OCH₃) or P(O)(OCH₃)₂;

b) V, Z, W, W' are not all -H; and

c) when Z is -R^z, then at least one of V, W, and W' is not -H, alkyl, aralkyl, or heterocycloalkyl;

and pharmaceutically acceptable salts and prodrugs thereof and pharmaceutically
20 acceptable salts of said prodrugs.

203. The method of claim 100 wherein said phosphonic acid-containing compound is a compound of Formula III:



wherein:

25 G is selected from the group consisting of -O-, -S-, -S(=O)-, -S(=O)₂-, -CH₂-, -CF₂-, -CHF-, -C(O)-, -CH(OH)-, -NH-, and -N(C₁-C₄ alkyl)-;

T is selected from the group consisting of -(CR^a₂)_k-, -CR^b=CR^b-(CR^a₂)_n-, -(CR^a₂)_n-CR^b=CR^b-, -(CR^a₂)_n-CR^b=CR^b-(CR^a₂)_n-, -O(CR^b₂)(CR^a₂)_n-, -S(CR^b₂)(CR^a₂)_n-, -N(R^c)(CR^b₂)(CR^a₂)_n-, -N(R^b)C(O)(CR^a₂)_n-,

$-(\text{CR}^a_2)_n\text{CH}(\text{NR}^b\text{R}^c)-$, $-\text{C}(\text{O})(\text{CR}^a_2)_m-$, $-(\text{CR}^a_2)_m\text{C}(\text{O})-$, $-(\text{CR}^a_2)\text{C}(\text{O})(\text{CR}^a_2)_n-$,
 $-(\text{CR}^a_2)_n\text{C}(\text{O})(\text{CR}^a_2)-$, and $-\text{C}(\text{O})\text{NH}(\text{CR}^b_2)(\text{CR}^a_2)_p-$;

k is an integer from 0-4;

m is an integer from 0-3;

5 n is an integer from 0-2;

p is an integer from 0-1;

Each R^a is independently selected from the group consisting of hydrogen, optionally substituted $-\text{C}_1-\text{C}_4$ alkyl, halogen, $-\text{OH}$, optionally substituted $-\text{O}-\text{C}_1-\text{C}_4$ alkyl, $-\text{OCF}_3$, optionally substituted $-\text{S}-\text{C}_1-\text{C}_4$ alkyl, $-\text{NR}^b\text{R}^c$, optionally substituted $-\text{C}_2-\text{C}_4$ alkenyl, and optionally substituted $-\text{C}_2-\text{C}_4$ alkynyl; with the proviso
 10 that when one R^a is attached to C through an O, S, or N atom, then the other R^a attached to the same C is a hydrogen, or attached via a carbon atom;

Each R^b is independently selected from the group consisting of hydrogen and optionally substituted $-\text{C}_1-\text{C}_4$ alkyl;

15 Each R^c is independently selected from the group consisting of hydrogen, optionally substituted $-\text{C}_1-\text{C}_4$ alkyl, optionally substituted $-\text{C}(\text{O})-\text{C}_1-\text{C}_4$ alkyl, and $-\text{C}(\text{O})\text{H}$;

R^1 and R^2 are each independently selected from the group consisting of halogen, optionally substituted $-\text{C}_1-\text{C}_4$ alkyl, optionally substituted $-\text{S}-\text{C}_1-\text{C}_3$ alkyl, optionally substituted $-\text{C}_2-\text{C}_4$ alkenyl, optionally substituted $-\text{C}_2-\text{C}_4$ alkynyl, $-\text{CF}_3$, $-\text{OCF}_3$, optionally substituted $-\text{O}-\text{C}_1-\text{C}_3$ alkyl, and cyano;

R^3 and R^4 are each independently selected from the group consisting of hydrogen, halogen, $-\text{CF}_3$, $-\text{OCF}_3$, cyano, optionally substituted $-\text{C}_1-\text{C}_{12}$ alkyl, optionally substituted $-\text{C}_2-\text{C}_{12}$ alkenyl, optionally substituted $-\text{C}_2-\text{C}_{12}$ alkynyl, optionally substituted $-(\text{CR}^a_2)_m$ aryl, optionally substituted $-(\text{CR}^a_2)_m$ cycloalkyl, optionally substituted $(\text{CR}^a_2)_m$ heterocycloalkyl, $-\text{OR}^d$, $-\text{SR}^d$, $-\text{S}(=\text{O})\text{R}^e$, $-\text{S}(=\text{O})_2\text{R}^e$, $-\text{S}(=\text{O})_2\text{NR}^f\text{R}^g$, $-\text{C}(\text{O})\text{NR}^f\text{R}^g$, $-\text{C}(\text{O})\text{OR}^h$, $-\text{C}(\text{O})\text{R}^e$, $-\text{N}(\text{R}^b)\text{C}(\text{O})\text{R}^e$, $-\text{N}(\text{R}^b)\text{C}(\text{O})\text{NR}^f\text{R}^g$, $-\text{N}(\text{R}^b)\text{S}(=\text{O})_2\text{R}^e$, $-\text{N}(\text{R}^b)\text{S}(=\text{O})_2\text{NR}^f\text{R}^g$, and $-\text{NR}^f\text{R}^g$;

Each R^d is selected from the group consisting of optionally substituted $-\text{C}_1-\text{C}_{12}$ alkyl, optionally substituted $-\text{C}_2-\text{C}_{12}$ alkenyl, optionally substituted $-\text{C}_2-\text{C}_{12}$ alkynyl, optionally substituted $-(\text{CR}^b_2)_n$ aryl, optionally substituted $-(\text{CR}^b_2)_n$ cycloalkyl, optionally substituted $-(\text{CR}^b_2)_n$ heterocycloalkyl, and $-\text{C}(\text{O})\text{NR}^f\text{R}^g$;

Each R^e is optionally substituted $-\text{C}_1-\text{C}_{12}$ alkyl, optionally substituted $-\text{C}_2-\text{C}_{12}$ alkenyl, optionally substituted $-\text{C}_2-\text{C}_{12}$ alkynyl, optionally substituted $-(\text{CR}^a_2)_n$ aryl,

optionally substituted $-(CR^a)_n$ cycloalkyl, and optionally substituted $-(CR^a)_n$ heterocycloalkyl;

R^f and R^g are each independently selected from the group consisting of hydrogen, optionally substituted $-C_1-C_{12}$ alkyl, optionally substituted $-C_2-C_{12}$ alkenyl, optionally substituted $-C_2-C_{12}$ alkynyl, optionally substituted $-(CR^b)_n$ aryl, optionally substituted $-(CR^b)_n$ cycloalkyl, and optionally substituted $-(CR^b)_n$ heterocycloalkyl, or R^f and R^g may together form an optionally substituted heterocyclic ring, which may contain a second heterogroup selected from the group of O, NR^c , and S, wherein said optionally substituted heterocyclic ring may be substituted with 0-4 substituents selected from the group consisting of optionally substituted $-C_1-C_4$ alkyl, $-OR^b$, oxo, cyano, $-CF_3$, optionally substituted phenyl, and $-C(O)OR^h$;

Each R^h is selected from the group consisting of optionally substituted $-C_1-C_{12}$ alkyl, optionally substituted $-C_2-C_{12}$ alkenyl, optionally substituted $-C_2-C_{12}$ alkynyl, optionally substituted $-(CR^b)_n$ aryl, optionally substituted $-(CR^b)_n$ cycloalkyl, and optionally substituted $-(CR^b)_n$ heterocycloalkyl;

R^5 is selected from the group consisting of $-OH$, optionally substituted $-OC_1-C_6$ alkyl, $-OC(O)R^e$, $-OC(O)OR^h$, $-F$, $-NHC(O)R^e$, $-NHS(=O)_2R^e$, $-NHS(=O)R^e$, $-NHC(=S)NH(R^h)$, and $-NHC(O)NH(R^h)$;

R^7 is selected from the group consisting of hydrogen, halogen, amino, hydroxyl, $-O-C_1-C_4$ alkyl, $-SH$ and $-S-C_1-C_4$ alkyl;

X is $P(O)YR^{11}Y'R^{11}$;

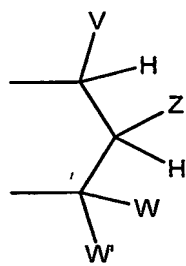
Y and Y' are each independently selected from the group consisting of $-O-$, and $-NR^v-$; when Y and Y' are $-O-$, R^{11} attached to $-O-$ is independently selected from the group consisting of $-H$, alkyl, optionally substituted aryl, optionally substituted heterocycloalkyl, optionally substituted CH_2 -heterocycloalkyl wherein the cyclic moiety contains a carbonate or thiocarbonate, optionally substituted $-alkylaryl$, $-C(R^z)_2OC(O)NR^z$, $-NR^z-C(O)-R^y$, $-C(R^z)_2-OC(O)R^y$, $-C(R^z)_2-O-C(O)OR^y$, $-C(R^z)_2OC(O)SR^y$, $-alkyl-S-C(O)R^y$, $-alkyl-S-S-alkylhydroxy$, and $-alkyl-S-S-S-alkylhydroxy$;

when Y and Y' are $-NR^v-$, then R^{11} attached to $-NR^v-$ is independently selected from the group consisting of $-H$, $-[C(R^z)_2]_q-COOR^y$, $-C(R^x)_2COOR^y$, $-[C(R^z)_2]_q-C(O)SR^y$, and $-cycloalkylene-COOR^y$;

when Y is -O- and Y' is NR^v, then R¹¹ attached to -O- is independently selected from the group consisting of -H, alkyl, optionally substituted aryl, optionally substituted heterocycloalkyl, optionally substituted CH₂-heterocycloalkyl wherein the cyclic moiety contains a carbonate or thiocarbonate, optionally

- 5 substituted -alkylaryl, -C(R^z)₂OC(O)NR^z, -NR^z-C(O)-R^y, -C(R^z)₂-OC(O)R^y, -C(R^z)₂-O-C(O)OR^y, -C(R^z)₂OC(O)SR^y, -alkyl-S-C(O)R^y, -alkyl-S-S-alkylhydroxy, and -alkyl-S-S-S-alkylhydroxy; and R¹¹ attached to -NR^v- is independently selected from the group consisting of -H, -[C(R^z)₂]_q-COOR^y, -C(R^x)₂COOR^y, -[C(R^z)₂]_q-C(O)SR^y, and -cycloalkylene-COOR^y;

- 10 or when Y and Y' are independently selected from -O- and -NR^v-, then together R¹¹ and R¹¹ are -alkyl-S-S-alkyl- to form a cyclic group, or together R¹¹ and R¹¹ are the group:



wherein:

- 15 V, W, and W' are independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted aralkyl, heterocycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, optionally substituted 1-alkenyl, and optionally substituted 1-alkynyl;

- or together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 atoms, wherein 0 – 1 atoms are heteroatoms and the remaining atoms are carbon, substituted with hydroxy, acyloxy, alkylthiocarbonyloxy, alkoxy carbonyloxy, or aryloxy carbonyloxy attached to a carbon atom that is three atoms from both Y groups attached to the phosphorus; or

- 20 or together V and Z are connected via an additional 3-5 atoms to form a cyclic group, wherein 0–1 atoms are heteroatoms and the remaining atoms are carbon, that is fused to an aryl group at the beta and gamma position to the Y attached to the phosphorus;

or together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to one of said carbon atoms that
 5 is three atoms from a Y attached to the phosphorus;

or together Z and W are connected via an additional 3-5 atoms to form a cyclic group, wherein 0-1 atoms are heteroatoms and the remaining atoms are carbon, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

or together W and W' are connected via an additional 2-5 atoms to form a cyclic
 10 group, wherein 0-2 atoms are heteroatoms and the remaining atoms are carbon, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

Z is selected from the group consisting of $-\text{CHR}^z\text{OH}$, $-\text{CHR}^z\text{OC(O)R}^y$, $-\text{CHR}^z\text{OC(S)R}^y$, $-\text{CHR}^z\text{OC(S)OR}^y$, $-\text{CHR}^z\text{OC(O)SR}^y$, $-\text{CHR}^z\text{OCO}_2\text{R}^y$, $-\text{OR}^z$, $-\text{SR}^z$, $-\text{CHR}^z\text{N}_3$, $-\text{CH}_2\text{aryl}$, $-\text{CH(aryl)OH}$, $-\text{CH(CH=CR}^z_2)\text{OH}$, $-\text{CH(C}\equiv\text{CR}^z)\text{OH}$,
 15 $-\text{R}^z$, $-\text{NR}^z_2$, $-\text{OCOR}^y$, $-\text{OCO}_2\text{R}^y$, $-\text{SCOR}^y$, $-\text{SCO}_2\text{R}^y$, $-\text{NHCOR}^z$, $-\text{NHCO}_2\text{R}^y$, $-\text{CH}_2\text{NHaryl}$, $-(\text{CH}_2)_q-\text{OR}^z$, and $-(\text{CH}_2)_q-\text{SR}^z$;

q is an integer 2 or 3;

Each R^z is selected from the group consisting of R^y and $-\text{H}$;

Each R^y is selected from the group consisting of alkyl, aryl, heterocycloalkyl, and
 20 aralkyl;

Each R^x is independently selected from the group consisting of $-\text{H}$, and alkyl, or together R^x and R^x form a cyclic alkyl group;

Each R^v is selected from the group consisting of $-\text{H}$, lower alkyl, acyloxyalkyl, alkoxycarbonyloxyalkyl, and lower acyl;

25 with the provisos that:

a) when G is selected from the group consisting of $-\text{O}-$, $-\text{S}-$, $-\text{S(=O)}-$, $-\text{S(=O)}_2-$, $-\text{CH}_2$, C(O) and $-\text{NR}^b$; T is $-\text{A-B}-$ where A is selected from the group consisting of $-\text{NR}^b$, $-\text{O}-$, $-\text{CH}_2-$ and $-\text{S}-$ and B is selected from the group consisting of a bond and substituted or unsubstituted C_1 - C_3 alkyl; R^3 is selected from the group consisting of
 30 halogen, trifluoromethyl, substituted or unsubstituted C_1 - C_6 alkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, aryloxy, substituted amide, sulfone, sulfonamide and C_3 - C_7 cycloalkyl, wherein said aryl, heteroaryl or cycloalkyl ring(s) are attached or fused to the aromatic; R^4 is selected from the group consisting of hydrogen, halogen, substituted or unsubstituted C_1 - C_6 alkyl, substituted or unsubstituted

aryl, and substituted or unsubstituted heteroaryl; R^1 and R^2 are each independently selected from the group consisting of halogen, substituted or unsubstituted C_1 - C_4 alkyl, and substituted or unsubstituted C_3 - C_5 cycloalkyl; R^7 is selected from the group consisting of hydrogen, halogen, amino, hydroxyl, -O- C_1 - C_4 alkyl, -SH and -S- C_1 - C_4 alkyl; and R^5 is selected from the group consisting of hydroxyl, optionally substituted -OC₁-C₆ alkyl, and -OC(O) R^e ; then X is not -P(O)(OH)₂;

c) V, Z, W, W' are not all -H; and

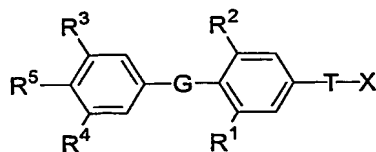
d) when Z is - R^z , then at least one of V, W, and W' is not -H, alkyl, aralkyl, or heterocycloalkyl;

10 and pharmaceutically acceptable salts and prodrugs thereof and pharmaceutically acceptable salts of said prodrugs.

204. The method of claim 202 wherein when G is -O-, T is -NH-CH₂-, R^1 and R^2 are each chloro, R^3 is *iso*-propyl, R^7 is fluoro and R^5 is -OH, then R^4 is not hydrogen.

205. The method of claim 203 wherein when G is selected from the group consisting of -O-, -S-, -S(=O)-, -S(=O)₂-, -CH₂-, -C(O)- and -NR^b-; T is -A-B- where A is selected from the group consisting of -NR^b-, -O-, -CH₂- and -S- and B is selected from the group consisting of a bond and substituted or unsubstituted C_1 - C_3 alkyl; R^3 is selected from the group consisting of halogen, trifluoromethyl, substituted or unsubstituted C_1 - C_6 alkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, aryloxy, substituted amide, sulfone, sulfonamide and C_3 - C_7 cycloalkyl, wherein said aryl, heteroaryl or cycloalkyl ring(s) are attached or fused to the aromatic; R^4 is selected from the group consisting of hydrogen, halogen, substituted or unsubstituted C_1 - C_6 alkyl, substituted or unsubstituted aryl, and substituted or unsubstituted heteroaryl; R^1 and R^2 are each independently selected from the group consisting of halogen, substituted or unsubstituted C_1 - C_4 alkyl, and substituted or unsubstituted C_3 - C_5 cycloalkyl; and R^7 is selected from the group consisting of hydrogen, halogen, amino, hydroxyl, -O- C_1 - C_4 alkyl, -SH and -S- C_1 - C_4 alkyl; then R^5 is not hydroxyl, optionally substituted -OC₁-C₆ alkyl, or -OC(O) R^e .

206. A pharmaceutical composition comprising a pharmaceutically effective amount of a compound of Formula I:



wherein:

G is selected from the group consisting of -O-, -S-, -S(=O)-, -S(=O)₂-,
-CH₂-, -CF₂-, -CHF-, -C(O)-, -CH(OH)-, -NH-, and -N(C₁-C₄ alkyl)-;

5 T is selected from the group consisting of -(CR^a₂)_k-, -CR^b=CR^b-(CR^a₂)_n-,
-(CR^a₂)_n-CR^b=CR^b-, -(CR^a₂)_n-CR^b=CR^b-(CR^a₂)_n-, -O(CR^b₂)(CR^a₂)_n-,
-S(CR^b₂)(CR^a₂)_n-, -N(R^c)(CR^b₂)(CR^a₂)_n-, -N(R^b)C(O)(CR^a₂)_n-,
-(CR^a₂)_nCH(NR^bR^c)-, -C(O)(CR^a₂)_m-, -(CR^a₂)_mC(O)-, -(CR^a₂)C(O)(CR^a₂)_n-,
-(CR^a₂)_nC(O)(CR^a₂)_p-, and -C(O)NH(CR^b₂)(CR^a₂)_p-;

10 k is an integer from 0-4;

m is an integer from 0-3;

n is an integer from 0-2;

p is an integer from 0-1;

Each R^a is independently selected from the group consisting of hydrogen,
15 optionally substituted -C₁-C₄ alkyl, halogen, -OH, optionally substituted -O-C₁-C₄
alkyl, -OCF₃, optionally substituted -S-C₁-C₄ alkyl, -NR^bR^c, optionally
substituted -C₂-C₄ alkenyl, and optionally substituted -C₂-C₄ alkynyl; with the proviso
that when one R^a is attached to C through an O, S, or N atom, then the other R^a attached
to the same C is a hydrogen, or attached via a carbon atom;

20 Each R^b is independently selected from the group consisting of hydrogen and
optionally substituted -C₁-C₄ alkyl;

Each R^c is independently selected from the group consisting of hydrogen and
optionally substituted -C₁-C₄ alkyl, optionally substituted -C(O)-C₁-C₄ alkyl,
and -C(O)H;

25 R¹ and R² are each independently selected from the group consisting of halogen,
optionally substituted -C₁-C₄ alkyl, optionally substituted -S-C₁-C₃ alkyl, optionally
substituted -C₂-C₄ alkenyl, optionally substituted -C₂-C₄ alkynyl, -CF₃, -OCF₃, optionally
substituted -O-C₁-C₃ alkyl, and cyano;

30 R³ and R⁴ are each independently selected from the group consisting of hydrogen,
halogen, -CF₃, -OCF₃, cyano, optionally substituted -C₁-C₁₂ alkyl, optionally
substituted -C₂-C₁₂ alkenyl, optionally substituted -C₂-C₁₂ alkynyl, optionally

substituted $-(CR^a)_m$ aryl, optionally substituted $-(CR^a)_m$ cycloalkyl, optionally substituted $-(CR^a)_m$ heterocycloalkyl, $-OR^d$, $-SR^d$, $-S(=O)R^e$, $-S(=O)_2R^e$, $-S(=O)_2NR^fR^g$, $-C(O)NR^fR^g$, $-C(O)OR^h$, $-C(O)R^e$, $-N(R^b)C(O)R^e$, $-N(R^b)C(O)NR^fR^g$, $-N(R^b)S(=O)_2R^e$, $-N(R^b)S(=O)_2NR^fR^g$, and $-NR^fR^g$;

- 5 Each R^d is selected from the group consisting of optionally substituted $-C_1$ - C_{12} alkyl, optionally substituted $-C_2$ - C_{12} alkenyl, optionally substituted $-C_2$ - C_{12} alkynyl, optionally substituted $-(CR^b)_n$ aryl, optionally substituted $-(CR^b)_n$ cycloalkyl, optionally substituted $-(CR^b)_n$ heterocycloalkyl, and $-C(O)NR^fR^g$;

- Each R^e is selected from the group consisting of optionally substituted $-C_1$ - C_{12} alkyl, optionally substituted $-C_2$ - C_{12} alkenyl, optionally substituted $-C_2$ - C_{12} alkynyl, 10 optionally substituted $-(CR^a)_n$ aryl, optionally substituted $-(CR^a)_n$ cycloalkyl, and optionally substituted $-(CR^a)_n$ heterocycloalkyl;

- R^f and R^g are each independently selected from the group consisting of hydrogen, optionally substituted $-C_1$ - C_{12} alkyl, optionally substituted $-C_2$ - C_{12} alkenyl, optionally substituted $-C_2$ - C_{12} alkynyl, 15 optionally substituted $-(CR^b)_n$ aryl, optionally substituted $-(CR^b)_n$ cycloalkyl, and optionally substituted $-(CR^b)_n$ heterocycloalkyl, or R^f and R^g may together form an optionally substituted heterocyclic ring, which may contain a second heterogroup selected from the group consisting of O, NR^c , and S, wherein said optionally substituted heterocyclic ring may be substituted with 0-4 substituents selected 20 from the group consisting of optionally substituted $-C_1$ - C_4 alkyl, $-OR^b$, oxo, cyano, $-CF_3$, optionally substituted phenyl, and $-C(O)OR^h$;

- Each R^h is selected from the group consisting of optionally substituted $-C_1$ - C_{12} alkyl, optionally substituted $-C_2$ - C_{12} alkenyl, optionally substituted $-C_2$ - C_{12} alkynyl, optionally substituted $-(CR^b)_n$ aryl, optionally substituted $-(CR^b)_n$ cycloalkyl, and 25 optionally substituted $-(CR^b)_n$ heterocycloalkyl;

R^5 is selected from the group consisting of $-OH$, optionally substituted $-OC_1$ - C_6 alkyl, $-OC(O)R^e$, $-OC(O)OR^h$, $-F$, $-NHC(O)R^e$, $-NHS(=O)R^e$, $-NHS(=O)_2R^e$, $-NHC(=S)NH(R^h)$, and $-NHC(O)NH(R^h)$;

X is $P(O)YR^{11}Y'R^{11}$;

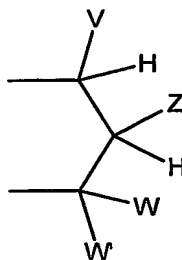
- 30 Y and Y' are each independently selected from the group consisting of $-O-$, and $-NR^v-$; when Y and Y' are $-O-$, R^{11} attached to $-O-$ is independently selected from the group consisting of $-H$, alkyl, optionally substituted aryl, optionally substituted heterocycloalkyl, optionally substituted CH_2 -heterocycloalkyl wherein the cyclic moiety contains a carbonate or thiocarbonate, optionally substituted $-alkylaryl$,

$-C(R^Z)_2OC(O)NR^Z$, $-NR^Z-C(O)-R^Y$, $-C(R^Z)_2-OC(O)R^Y$,
 $-C(R^Z)_2-O-C(O)OR^Y$, $-C(R^Z)_2OC(O)SR^Y$, $-alkyl-S-C(O)R^Y$, $-alkyl-S-S-alkylhydroxy$,
 and $-alkyl-S-S-S-alkylhydroxy$;

when Y and Y' are $-NR^V$ -, then R^{11} attached to $-NR^V$ - is independently selected
 5 from the group consisting
 of $-H$, $-[C(R^Z)_2]_q-COOR^Y$, $-C(R^X)_2COOR^Y$, $-[C(R^Z)_2]_q-C(O)SR^Y$,
 and $-cycloalkylene-COOR^Y$;

when Y is $-O-$ and Y' is NR^V , then R^{11} attached to $-O-$ is independently selected
 from the group consisting of $-H$, alkyl, optionally substituted aryl, optionally substituted
 10 heterocycloalkyl, optionally substituted CH_2 -heterocycloalkyl wherein the cyclic moiety
 contains a carbonate or thiocarbonate, optionally
 substituted $-alkylaryl$, $-C(R^Z)_2OC(O)NR^Z$, $-NR^Z-C(O)-R^Y$, $-C(R^Z)_2-OC(O)R^Y$,
 $-C(R^Z)_2-O-C(O)OR^Y$, $-C(R^Z)_2OC(O)SR^Y$, $-alkyl-S-C(O)R^Y$, $-alkyl-S-S-alkylhydroxy$,
 and $-alkyl-S-S-S-alkylhydroxy$; and R^{11} attached to $-NR^V$ - is independently selected from
 15 the group consisting of $-H$, $-[C(R^Z)_2]_q-COOR^Y$, $-C(R^X)_2COOR^Y$, $-[C(R^Z)_2]_q-C(O)SR^Y$,
 and $-cycloalkylene-COOR^Y$;

or when Y and Y' are independently selected from $-O-$ and $-NR^V$ -, then together
 R^{11} and R^{11} are $-alkyl-S-S-alkyl-$ to form a cyclic group, or together R^{11} and R^{11} are the
 group:



20

wherein:

V, W, and W' are independently selected from the group consisting of hydrogen,
 optionally substituted alkyl, optionally substituted aralkyl, heterocycloalkyl, aryl,
 substituted aryl, heteroaryl, substituted heteroaryl, optionally substituted 1-alkenyl, and
 25 optionally substituted 1-alkynyl;

or together V and Z are connected via an additional 3-5 atoms to form a cyclic
 group containing 5-7 atoms, wherein 0-1 atoms are heteroatoms and the remaining
 atoms are carbon, substituted with hydroxy, acyloxy, alkylthiocarbonyloxy,

alkoxycarbonyloxy, or aryloxycarbonyloxy attached to a carbon atom that is three atoms from both Y groups attached to the phosphorus; or

or together V and Z are connected via an additional 3-5 atoms to form a cyclic group, wherein 0-1 atoms are heteroatoms and the remaining atoms are carbon, that is fused to an aryl group at the beta and gamma position to the Y attached to the phosphorus;

or together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to one of said carbon atoms that is three atoms from a Y attached to the phosphorus;

or together Z and W are connected via an additional 3-5 atoms to form a cyclic group, wherein 0-1 atoms are heteroatoms and the remaining atoms are carbon, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

or together W and W' are connected via an additional 2-5 atoms to form a cyclic group, wherein 0-2 atoms are heteroatoms and the remaining atoms are carbon, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

Z is selected from the group consisting of $-\text{CHR}^z\text{OH}$, $-\text{CHR}^z\text{OC}(\text{O})\text{R}^y$, $-\text{CHR}^z\text{OC}(\text{S})\text{R}^y$, $-\text{CHR}^z\text{OC}(\text{S})\text{OR}^y$, $-\text{CHR}^z\text{OC}(\text{O})\text{SR}^y$, $-\text{CHR}^z\text{OCO}_2\text{R}^y$, $-\text{OR}^z$, $-\text{SR}^z$, $-\text{CHR}^z\text{N}_3$, $-\text{CH}_2\text{aryl}$, $-\text{CH}(\text{aryl})\text{OH}$, $-\text{CH}(\text{CH}=\text{CR}^z_2)\text{OH}$, $-\text{CH}(\text{C}\equiv\text{CR}^z_2)\text{OH}$, $-\text{R}^z$, $-\text{NR}^z_2$, $-\text{OCOR}^y$, $-\text{OCO}_2\text{R}^y$, $-\text{SCOR}^y$, $-\text{SCO}_2\text{R}^y$, $-\text{NHCOR}^z$, $-\text{NHCO}_2\text{R}^y$, $-\text{CH}_2\text{NHaryl}$, $-(\text{CH}_2)_q-\text{OR}^z$, and $-(\text{CH}_2)_q-\text{SR}^z$;

q is an integer 2 or 3;

Each R^z is selected from the group consisting of R^y and $-\text{H}$;

Each R^y is selected from the group consisting of alkyl, aryl, heterocycloalkyl, and aralkyl;

Each R^x is independently selected from the group consisting of $-\text{H}$, and alkyl, or together R^x and R^x form a cyclic alkyl group;

Each R^v is selected from the group consisting of $-\text{H}$, lower alkyl, acyloxyalkyl, alkoxycarbonyloxyalkyl, and lower acyl;

with the provisos that:

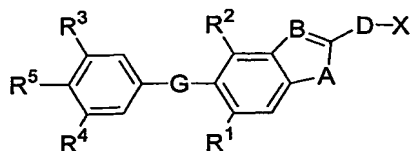
a) V, Z, W, W' are not all $-\text{H}$; and

b) when Z is $-\text{R}^z$, then at least one of V, W, and W' is not $-\text{H}$, alkyl, aralkyl, or heterocycloalkyl;

and pharmaceutically acceptable salts and prodrugs thereof and pharmaceutically acceptable salts of said prodrugs

and a pharmaceutically acceptable carrier.

207. A pharmaceutical composition comprising a pharmaceutically effective
5 amount of a compound of Formula II:



wherein:

A is selected from the group consisting of -NRⁱ-, -O-, and -S-;

B is selected from the group consisting of -CR^b-, and -N-;

10 Rⁱ is selected from the group consisting of hydrogen, -C(O)C₁-C₄ alkyl, -C₁-C₄ alkyl, and -C₁-C₄-aryl;

R^b is selected from the group consisting of hydrogen and optionally substituted -C₁-C₄ alkyl;

15 G is selected from the group consisting of -O-, -S-, -S(=O)-, -S(=O)₂-, -CH₂-, -CF₂-, -CHF-, -C(O)-, -CH(OH)-, -NH-, and -N(C₁-C₄ alkyl)-;

D is selected from the group consisting of a bond, -(CR^a)₂-, and -C(O)-;

Each R^a is independently selected from the group consisting of hydrogen, optionally substituted -C₁-C₄ alkyl, halogen, -OH, optionally substituted -O-C₁-C₄ alkyl, -OCF₃, optionally substituted -S-C₁-C₄ alkyl, -NR^bR^c, optionally
20 substituted -C₂-C₄ alkenyl, and optionally substituted -C₂-C₄ alkynyl; with the proviso that when one R^a is attached to C through an O, S, or N atom, then the other R^a attached to the same C is a hydrogen, or attached via a carbon atom;

R¹ and R² are each independently selected from the group consisting of halogen, optionally substituted -C₁-C₄ alkyl, optionally substituted -S-C₁-C₃ alkyl, optionally
25 substituted -C₂-C₄ alkenyl, optionally substituted -C₂-C₄ alkynyl, -CF₃, -OCF₃, optionally substituted -O-C₁-C₃ alkyl, and cyano;

R³ and R⁴ are each independently selected from the group consisting of hydrogen, halogen, -CF₃, -OCF₃, cyano, optionally substituted -C₁-C₁₂ alkyl, optionally substituted -C₂-C₁₂ alkenyl, optionally substituted -C₂-C₁₂ alkynyl, optionally
30 substituted -(CR^a)_maryl, optionally substituted -(CR^a)_mcycloalkyl, optionally

substituted $-(CR^a)_m$ heterocycloalkyl, $-OR^d$, $-SR^d$, $-S(=O)R^e$, $-S(=O)_2R^e$, $-S(=O)_2NR^fR^g$, $-C(O)NR^fR^g$, $-C(O)OR^h$, $-C(O)R^e$, $-N(R^b)C(O)R^e$, $-N(R^b)C(O)NR^fR^g$, $-N(R^b)S(=O)_2R^e$, $-N(R^b)S(=O)_2NR^fR^g$, and $-NR^fR^g$;

Each R^d is selected from the group consisting of optionally substituted $-C_1-C_{12}$ alkyl, optionally substituted $-C_2-C_{12}$ alkenyl, optionally substituted $-C_2-C_{12}$ alkynyl, optionally substituted $-(CR^b)_n$ aryl, optionally substituted $-(CR^b)_n$ cycloalkyl, optionally substituted $-(CR^b)_n$ heterocycloalkyl, and $-C(O)NR^fR^g$;

Each R^e is selected from the group consisting of optionally substituted $-C_1-C_{12}$ alkyl, optionally substituted $-C_2-C_{12}$ alkenyl, optionally substituted $-C_2-C_{12}$ alkynyl, optionally substituted $-(CR^a)_n$ aryl, optionally substituted $-(CR^a)_n$ cycloalkyl, and optionally substituted $-(CR^a)_n$ heterocycloalkyl;

R^f and R^g are each independently selected from the group consisting of hydrogen, optionally substituted $-C_1-C_{12}$ alkyl, optionally substituted $-C_2-C_{12}$ alkenyl, optionally substituted $-C_2-C_{12}$ alkynyl, optionally substituted $-(CR^b)_n$ aryl, optionally substituted $-(CR^b)_n$ cycloalkyl, and optionally substituted $-(CR^b)_n$ heterocycloalkyl, or R^f and R^g may together form an optionally substituted heterocyclic ring, which may contain a second heterogroup selected from the group consisting of O, NR^e , and S, wherein said optionally substituted heterocyclic ring may be substituted with 0-4 substituents selected from the group consisting of optionally substituted $-C_1-C_4$ alkyl, $-OR^b$, oxo, cyano, $-CF_3$, optionally substituted phenyl, and $-C(O)OR^h$;

Each R^h is selected from the group consisting of optionally substituted $-C_1-C_{12}$ alkyl, optionally substituted $-C_2-C_{12}$ alkenyl, optionally substituted $-C_2-C_{12}$ alkynyl, optionally substituted $-(CR^b)_n$ aryl, optionally substituted $-(CR^b)_n$ cycloalkyl, and optionally substituted $-(CR^b)_n$ heterocycloalkyl;

R^5 is selected from the group consisting of $-OH$, optionally substituted $-OC_1-C_6$ alkyl, $-OC(O)R^e$, $-OC(O)OR^h$, $-F$, $-NHC(O)R^e$, $-NHS(=O)R^e$, $-NHS(=O)_2R^e$, $-NHC(=S)NH(R^h)$, and $-NHC(O)NH(R^h)$;

X is $P(O)YR^{11}Y'R^{11}$;

Y and Y' are each independently selected from the group consisting of $-O-$, and $-NR^v-$; when Y and Y' are $-O-$, R^{11} attached to $-O-$ is independently selected from the group consisting of $-H$, alkyl, optionally substituted aryl, optionally substituted heterocycloalkyl, optionally substituted CH_2 -heterocycloalkyl wherein the cyclic moiety contains a carbonate or thiocarbonate, optionally substituted $-alkylaryl$, $-C(R^z)_2OC(O)NR^z$, $-NR^z-C(O)-R^y$, $-C(R^z)_2-OC(O)R^y$,

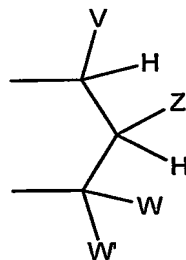
-C(R^z)₂-O-C(O)OR^y, -C(R^z)₂OC(O)SR^y, -alkyl-S-C(O)R^y, -alkyl-S-S-alkylhydroxy, and -alkyl-S-S-S-alkylhydroxy;

when Y and Y' are -NR^v-, then R¹¹ attached to -NR^v- is independently selected from the group consisting

- 5 of -H, -[C(R^z)₂]_q-COOR^y, -C(R^x)₂COOR^y, -[C(R^z)₂]_q-C(O)SR^y, and -cycloalkylene-COOR^y;

- when Y is -O- and Y' is NR^v-, then R¹¹ attached to -O- is independently selected from the group consisting of -H, alkyl, optionally substituted aryl, optionally substituted heterocycloalkyl, optionally substituted CH₂-heterocycloalkyl wherein the cyclic moiety
10 contains a carbonate or thiocarbonate, optionally substituted -alkylaryl, -C(R^z)₂OC(O)NR^z, -NR^z-C(O)-R^y, -C(R^z)₂-OC(O)R^y, -C(R^z)₂-O-C(O)OR^y, -C(R^z)₂OC(O)SR^y, -alkyl-S-C(O)R^y, -alkyl-S-S-alkylhydroxy, and -alkyl-S-S-S-alkylhydroxy; and R¹¹ attached to -NR^v- is independently selected from the group consisting of -H, -[C(R^z)₂]_q-COOR^y, -C(R^x)₂COOR^y, -[C(R^z)₂]_q-C(O)SR^y,
15 and -cycloalkylene-COOR^y;

or when Y and Y' are independently selected from -O- and -NR^v-, then together R¹¹ and R¹¹ are -alkyl-S-S-alkyl- to form a cyclic group, or together R¹¹ and R¹¹ are the group:



- 20 wherein:

V, W, and W' are independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted aralkyl, heterocycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, optionally substituted 1-alkenyl, and optionally substituted 1-alkynyl;

- 25 or together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 atoms, wherein 0-1 atoms are heteroatoms and the remaining atoms are carbon, substituted with hydroxy, acyloxy, alkylthiocarbonyloxy,

alkoxycarbonyloxy, or aryloxy carbonyloxy attached to a carbon atom that is three atoms from both Y groups attached to the phosphorus; or

or together V and Z are connected via an additional 3-5 atoms to form a cyclic group, wherein 0-1 atoms are heteroatoms and the remaining atoms are carbon, that is fused to an aryl group at the beta and gamma position to the Y attached to the phosphorus;

or together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxy carbonyloxy, attached to one of said carbon atoms that is three atoms from a Y attached to the phosphorus;

or together Z and W are connected via an additional 3-5 atoms to form a cyclic group, wherein 0-1 atoms are heteroatoms and the remaining atoms are carbon, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

or together W and W' are connected via an additional 2-5 atoms to form a cyclic group, wherein 0-2 atoms are heteroatoms and the remaining atoms are carbon, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

Z is selected from the group consisting of $-\text{CHR}^z\text{OH}$, $-\text{CHR}^z\text{OC}(\text{O})\text{R}^y$, $-\text{CHR}^z\text{OC}(\text{S})\text{R}^y$, $-\text{CHR}^z\text{OC}(\text{S})\text{OR}^y$, $-\text{CHR}^z\text{OC}(\text{O})\text{SR}^y$, $-\text{CHR}^z\text{OCO}_2\text{R}^y$, $-\text{OR}^z$, $-\text{SR}^z$, $-\text{CHR}^z\text{N}_3$, $-\text{CH}_2\text{aryl}$, $-\text{CH}(\text{aryl})\text{OH}$, $-\text{CH}(\text{CH}=\text{CR}^z_2)\text{OH}$, $-\text{CH}(\text{C}\equiv\text{CR}^z)\text{OH}$, $-\text{R}^z$, $-\text{NR}^z_2$, $-\text{OCOR}^y$, $-\text{OCO}_2\text{R}^y$, $-\text{SCOR}^y$, $-\text{SCO}_2\text{R}^y$, $-\text{NHCOR}^z$, $-\text{NHCO}_2\text{R}^y$, $-\text{CH}_2\text{NHaryl}$, $-(\text{CH}_2)_q-\text{OR}^z$, and $-(\text{CH}_2)_q-\text{SR}^z$;

q is an integer 2 or 3;

Each R^z is selected from the group consisting of R^y and $-\text{H}$;

Each R^y is selected from the group consisting of alkyl, aryl, heterocycloalkyl, and aralkyl;

Each R^x is independently selected from the group consisting of $-\text{H}$, and alkyl, or together R^x and R^x form a cyclic alkyl group;

Each R^y is selected from the group consisting of $-\text{H}$, lower alkyl, acyloxyalkyl, alkoxycarbonyloxyalkyl, and lower acyl;

with the provisos that:

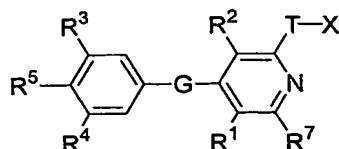
a) V, Z, W, W' are not all $-\text{H}$; and

b) when Z is $-\text{R}^z$, then at least one of V, W, and W' is not $-\text{H}$, alkyl, aralkyl, or heterocycloalkyl;

and pharmaceutically acceptable salts and prodrugs thereof and pharmaceutically acceptable salts of said prodrugs.

and a pharmaceutically acceptable carrier.

208. A pharmaceutical composition comprising a pharmaceutically effective
5 amount of a compound of Formula III:



wherein:

G is selected from the group consisting of -O-, -S-, -S(=O)-, -S(=O)₂-,
-CH₂-, -CF₂-, -CHF-, -C(O)-, -CH(OH)-, -NH-, and -N(C₁-C₄ alkyl)-;

10 T is selected from the group consisting of -(CR^a₂)_k-, -CR^b=CR^b-(CR^a₂)_n-,
-(CR^a₂)_n-CR^b=CR^b-, -(CR^a₂)_n-CR^b=CR^b-(CR^a₂)_n-,
-O(CR^b₂)(CR^a₂)_n-, -S(CR^b₂)(CR^a₂)_n-, -N(R^c)(CR^b₂)(CR^a₂)_n-, -N(R^b)C(O)(CR^a₂)_n-,
-(CR^a₂)_nCH(NR^bR^c)-, -C(O)(CR^a₂)_m-, -(CR^a₂)_mC(O)-, -(CR^a₂)C(O)(CR^a₂)_n-,
-(CR^a₂)_nC(O)(CR^a₂)_n-, and -C(O)NH(CR^b₂)(CR^a₂)_p-;

15 k is an integer from 0-4;

m is an integer from 0-3;

n is an integer from 0-2;

p is an integer from 0-1;

Each R^a is independently selected from the group consisting of hydrogen,
20 optionally substituted -C₁-C₄ alkyl, halogen, -OH, optionally substituted -O-C₁-C₄
alkyl, -OCF₃, optionally substituted -S-C₁-C₄ alkyl, -NR^bR^c, optionally
substituted -C₂-C₄ alkenyl, and optionally substituted -C₂-C₄ alkynyl; with the proviso
that when one R^a is attached to C through an O, S, or N atom, then the other R^a attached
to the same C is a hydrogen, or attached via a carbon atom;

25 Each R^b is independently selected from the group consisting of hydrogen and
optionally substituted -C₁-C₄ alkyl;

Each R^c is independently selected from the group consisting of hydrogen and
optionally substituted -C₁-C₄ alkyl, optionally substituted -C(O)-C₁-C₄ alkyl,
and -C(O)H;

R^1 and R^2 are each independently selected from the group consisting of halogen, optionally substituted $-C_1-C_4$ alkyl, optionally substituted $-S-C_1-C_3$ alkyl, optionally substituted $-C_2-C_4$ alkenyl, optionally substituted $-C_2-C_4$ alkynyl, $-CF_3$, $-OCF_3$, optionally substituted $-O-C_1-C_3$ alkyl, and cyano;

- 5 R^3 and R^4 are each independently selected from the group consisting of hydrogen, halogen, $-CF_3$, $-OCF_3$, cyano, optionally substituted $-C_1-C_{12}$ alkyl, optionally substituted $-C_2-C_{12}$ alkenyl, optionally substituted $-C_2-C_{12}$ alkynyl, optionally substituted $-(CR^a)_m$ aryl, optionally substituted $-(CR^a)_m$ cycloalkyl, optionally substituted $-(CR^a)_m$ heterocycloalkyl, $-OR^d$, $-SR^d$, $-S(=O)R^e$, $-S(=O)_2R^e$, $-S(=O)_2NR^fR^g$,
 10 $-C(O)NR^fR^g$, $-C(O)OR^h$, $-C(O)R^e$, $-N(R^b)C(O)R^e$, $-N(R^b)C(O)NR^fR^g$, $-N(R^b)S(=O)_2R^e$, $-N(R^b)S(=O)_2NR^fR^g$, and $-NR^fR^g$;

- Each R^d is selected from the group consisting of optionally substituted $-C_1-C_{12}$ alkyl, optionally substituted $-C_2-C_{12}$ alkenyl, optionally substituted $-C_2-C_{12}$ alkynyl, optionally substituted $-(CR^b)_n$ aryl, optionally substituted $-(CR^b)_n$ cycloalkyl, optionally substituted $-(CR^b)_n$ heterocycloalkyl, and $-C(O)NR^fR^g$;
- 15

Each R^e is selected from the group consisting of optionally substituted $-C_1-C_{12}$ alkyl, optionally substituted $-C_2-C_{12}$ alkenyl, optionally substituted $-C_2-C_{12}$ alkynyl, optionally substituted $-(CR^a)_n$ aryl, optionally substituted $-(CR^a)_n$ cycloalkyl, and optionally substituted $-(CR^a)_n$ heterocycloalkyl;

- 20 R^f and R^g are each independently selected from the group consisting of hydrogen, optionally substituted $-C_1-C_{12}$ alkyl, optionally substituted $-C_2-C_{12}$ alkenyl, optionally substituted $-C_2-C_{12}$ alkynyl, optionally substituted $-(CR^b)_n$ aryl, optionally substituted $-(CR^b)_n$ cycloalkyl, and optionally substituted $-(CR^b)_n$ heterocycloalkyl, or R^f and R^g may together form an optionally substituted heterocyclic ring, which may contain
 25 a second heterogroup selected from the group consisting of O, NR^c , and S, wherein said optionally substituted heterocyclic ring may be substituted with 0-4 substituents selected from the group consisting of optionally substituted $-C_1-C_4$ alkyl, $-OR^b$, oxo, cyano, $-CF_3$, optionally substituted phenyl, and $-C(O)OR^h$;

- Each R^h is selected from the group consisting of optionally substituted $-C_1-C_{12}$ alkyl, optionally substituted $-C_2-C_{12}$ alkenyl, optionally substituted $-C_2-C_{12}$ alkynyl, optionally substituted $-(CR^b)_n$ aryl, optionally substituted $-(CR^b)_n$ cycloalkyl, and optionally substituted $-(CR^b)_n$ heterocycloalkyl;
- 30

R^5 is selected from the group consisting of -OH, optionally substituted -OC₁-C₆ alkyl, -OC(O)R^e, -OC(O)OR^h, -F, -NHC(O)R^e, -NHS(=O)R^e, -NHS(=O)₂R^e, -NHC(=S)NH(R^h), and -NHC(O)NH(R^h);

R^7 is selected from the group consisting of hydrogen, halogen, amino, hydroxyl,
5 -O-C₁-C₄ alkyl, -SH and -S-C₁-C₄ alkyl;

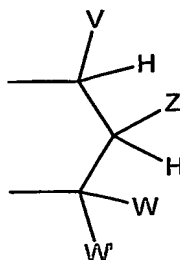
X is P(O)YR¹¹Y'R¹¹;

Y and Y' are each independently selected from the group consisting of -O-,
and -NR^v-; when Y and Y' are -O-, R¹¹ attached to -O- is independently selected from
the group consisting of -H, alkyl, optionally substituted aryl, optionally substituted
10 heterocycloalkyl, optionally substituted CH₂-heterocycloalkyl wherein the cyclic moiety
contains a carbonate or thiocarbonate, optionally substituted -alkylaryl,
-C(R^z)₂OC(O)NR^z₂, -NR^z-C(O)-R^y, -C(R^z)₂-OC(O)R^y,
-C(R^z)₂-O-C(O)OR^y, -C(R^z)₂OC(O)SR^y, -alkyl-S-C(O)R^y, -alkyl-S-S-alkylhydroxy,
and -alkyl-S-S-S-alkylhydroxy;

15 when Y and Y' are -NR^v-, then R¹¹ attached to -NR^v- is independently selected
from the group consisting
of -H, -[C(R^z)₂]_q-COOR^y, -C(R^x)₂COOR^y, -[C(R^z)₂]_q-C(O)SR^y,
and -cycloalkylene-COOR^y;

when Y is -O- and Y' is NR^v-, then R¹¹ attached to -O- is independently selected
20 from the group consisting of -H, alkyl, optionally substituted aryl, optionally substituted
heterocycloalkyl, optionally substituted CH₂-heterocycloalkyl wherein the cyclic moiety
contains a carbonate or thiocarbonate, optionally
substituted -alkylaryl, -C(R^z)₂OC(O)NR^z₂, -NR^z-C(O)-R^y, -C(R^z)₂-OC(O)R^y,
-C(R^z)₂-O-C(O)OR^y, -C(R^z)₂OC(O)SR^y, -alkyl-S-C(O)R^y, -alkyl-S-S-alkylhydroxy,
25 and -alkyl-S-S-S-alkylhydroxy; and R¹¹ attached to -NR^v- is independently selected from
the group consisting of -H, -[C(R^z)₂]_q-COOR^y, -C(R^x)₂COOR^y, -[C(R^z)₂]_q-C(O)SR^y,
and -cycloalkylene-COOR^y;

or when Y and Y' are independently selected from -O- and -NR^v-, then together
R¹¹ and R¹¹ are -alkyl-S-S-alkyl- to form a cyclic group, or together R¹¹ and R¹¹ are the
30 group:



wherein:

V, W, and W' are independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted aralkyl, heterocycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, optionally substituted 1-alkenyl, and optionally substituted 1-alkynyl;

or together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 atoms, wherein 0-1 atoms are heteroatoms and the remaining atoms are carbon, substituted with hydroxy, acyloxy, alkylthiocarbonyloxy, alkoxy carbonyloxy, or aryloxy carbonyloxy attached to a carbon atom that is three atoms from both Y groups attached to the phosphorus; or

or together V and Z are connected via an additional 3-5 atoms to form a cyclic group, wherein 0-1 atoms are heteroatoms and the remaining atoms are carbon, that is fused to an aryl group at the beta and gamma position to the Y attached to the phosphorus;

or together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxy carbonyloxy, alkylthiocarbonyloxy, and aryloxy carbonyloxy, attached to one of said carbon atoms that is three atoms from a Y attached to the phosphorus;

or together Z and W are connected via an additional 3-5 atoms to form a cyclic group, wherein 0-1 atoms are heteroatoms and the remaining atoms are carbon, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

or together W and W' are connected via an additional 2-5 atoms to form a cyclic group, wherein 0-2 atoms are heteroatoms and the remaining atoms are carbon, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

Z is selected from the group consisting of $-\text{CHR}^Z\text{OH}$, $-\text{CHR}^Z\text{OC}(\text{O})\text{R}^Y$, $-\text{CHR}^Z\text{OC}(\text{S})\text{R}^Y$, $-\text{CHR}^Z\text{OC}(\text{S})\text{OR}^Y$, $-\text{CHR}^Z\text{OC}(\text{O})\text{SR}^Y$, $-\text{CHR}^Z\text{OCO}_2\text{R}^Y$, $-\text{OR}^Z$,

-SR^z, -CHR^zN₃, -CH₂aryl, -CH(aryl)OH, -CH(CH=CR^z)OH, -CH(C≡CR^z)OH, -R^z, -NR^z, -OCOR^y, -OCO₂R^y, -SCOR^y, -SCO₂R^y, -NHCOR^z, -NHCO₂R^y, -CH₂NHaryl, -(CH₂)_q-OR^z, and -(CH₂)_q-SR^z;

q is an integer 2 or 3;

5 Each R^z is selected from the group consisting of R^y and -H;

Each R^y is selected from the group consisting of alkyl, aryl, heterocycloalkyl, and aralkyl;

Each R^x is independently selected from the group consisting of -H, and alkyl, or together R^x and R^x form a cyclic alkyl group;

10 Each R^v is selected from the group consisting of -H, lower alkyl, acyloxyalkyl, alkoxy carbonyloxyalkyl, and lower acyl;

with the provisos that:

a) V, Z, W, W' are not all -H; and

b) when Z is -R^z, then at least one of V, W, and W' is not -H, alkyl, aralkyl,

15 or heterocycloalkyl;

and pharmaceutically acceptable salts and prodrugs thereof and pharmaceutically acceptable salts of said prodrugs.

and a pharmaceutically acceptable carrier.

209. The pharmaceutical composition as in any of claims 206, 207, or 208
20 wherein said pharmaceutical composition is in the form of a controlled release composition.

210. The pharmaceutical composition as in any of claims 206, 207, or 208 wherein said pharmaceutical composition is in the form of a transdermal patch.

211. The pharmaceutical composition as in any of claims 206, 207, or 208
25 wherein said pharmaceutical composition is in the form of a tablet.

212. The pharmaceutical composition as in any of claims 206, 207, or 208 wherein said pharmaceutical composition is in the form of a hard capsule.

213. The pharmaceutical composition as in any of claims 206, 207, or 208 wherein said pharmaceutical composition is in the form of a soft capsule.

30 214. The pharmaceutical composition as in any of claims 206, 207, or 208 wherein said pharmaceutical composition comprises a crystalline form of said compound of Formula I, II, or III.

215. The pharmaceutical composition as in any of claims 206, 207, or 208 wherein said pharmaceutical composition comprises a salt form of said compound of Formula I, II, or III.

216. The pharmaceutical composition as in any of claims 206, 207, or 208
5 wherein said pharmaceutical composition is administered orally in a unit dose of about 0.375 µg/kg to 3.375 mg/kg.

217. The pharmaceutical composition of claim 216 wherein said unit dose is about 3.75 µg/kg to 0.375 mg/kg.

218. The pharmaceutical composition of claim 216 wherein said unit dose is
10 about 3.75 µg/kg to 37.5 µg/kg.

219. The pharmaceutical composition of claim 216 wherein said unit dose is about 3.75 µg/kg to 60 µg/kg.

220. The pharmaceutical composition of claim 216 wherein said unit dose is about 0.188 µg/kg to 1.88 mg/kg.

221. The pharmaceutical composition of claim 216 wherein said unit dose is
15 about 1.88 µg/kg to .188 mg/kg.

222. The pharmaceutical composition of claim 216 wherein said unit dose is about 1.88 µg/kg to 18.8 µg/kg.

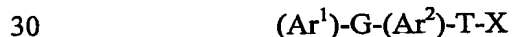
223. The pharmaceutical composition of claim 216 wherein said unit dose is
20 about 1.88 µg/kg to 30 µg/kg.

224. The pharmaceutical composition as in any of claims 206, 207, or 208 wherein said pharmaceutical composition is administered orally in a total daily dose of about 0.375 µg/kg/day to about 3.75 mg/kg/day, equivalent of the free acid.

225. The pharmaceutical composition of claim 224 wherein said total daily
25 dose is about 3.75 µg/kg/day to about 0.375 mg/kg/day, equivalent of the free acid.

226. The pharmaceutical composition of claim 224 wherein said total daily dose is about 30 µg/kg/day to about 3.0 mg/kg/day, equivalent of the free acid.

227. A phosphonic acid containing thyromimetic compound of Formula X:



wherein:

Ar¹ and Ar² are aryl groups;

G is an atom or group of atoms that links Ar¹ and Ar² through a single C, S, O, or N atom;

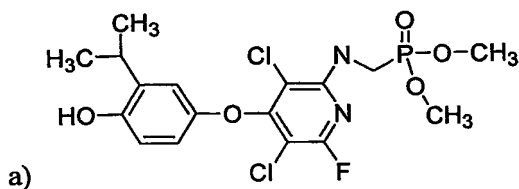
T is an atom or group of atoms linking Ar² to X through 1-4 contiguous atoms or is absent;

5 X is a -P(O)(OH)₂ or prodrug thereof;

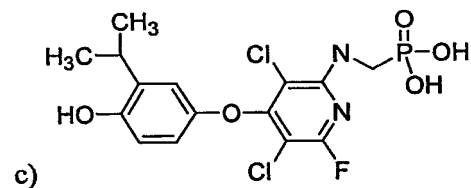
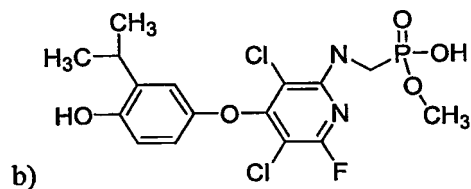
wherein (Ar¹)-G-(Ar²)-T-P(O)(OH)₂ has a Ki of ≤ 150 nM relative to T3;

with the provisos that said -P(O)(OH)₂ containing thryomimetic compound is

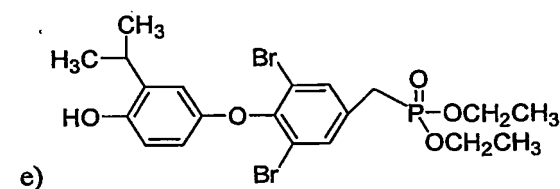
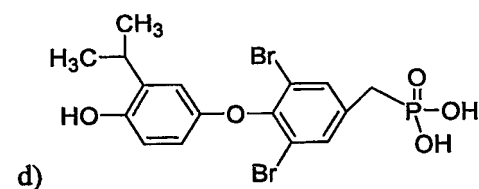
not:



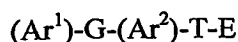
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228. A method of improving liver versus heart selectivity of a thyromimetic compound of Formula Y:



5

wherein:

Ar^1 and Ar^2 are aryl groups;

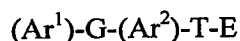
G is an atom or group of atoms that links Ar^1 and Ar^2 through a single C, S, O, or N atom;

10 T is an atom or group of atoms linking Ar^2 to E through 1-4 contiguous atoms or is absent;

E is selected from the group consisting of a functional group or moiety with a $pK_a \leq 7.4$, a carboxylic acid moiety or an atom or group of atoms containing an O or N that binds the thyroid hormone binding pocket of a $TR\alpha$ or $TR\beta$, comprising the step of
15 replacing E with a $-P(O)(OH)_2$ or prodrug thereof.

229. A method of increasing the therapeutic index of a thyromimetic compound of Formula Y:

20



wherein:

Ar^1 and Ar^2 are aryl groups;

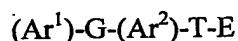
25 G is an atom or group of atoms that links Ar^1 and Ar^2 through a single C, S, O, or N atom;

T is an atom or group of atoms linking Ar^2 to E through 1-4 atoms or is absent;

E is selected from the group consisting of a functional group or moiety with a $pK_a \leq 7.4$, a carboxylic acid moiety or an atom or group of atoms containing an O or N that binds the thyroid hormone binding pocket of a $TR\alpha$ or $TR\beta$, comprising the step of
30 replacing E with a $-P(O)(OH)_2$ or prodrug thereof.

230. A method of designing a thyromimetic compound with improved liver versus heart selectivity comprising the steps of:

obtaining a molecular formula for a thyromimetic of Formula Y:



wherein:

5 Ar^1 and Ar^2 are aryl groups;

G is an atom or group of atoms that links Ar^1 and Ar^2 through a single C, S, O, or N atom;

T is an atom or group of atoms linking Ar^2 to E through 1-4 contiguous atoms or is absent;

10 E is selected from the group consisting of a functional group or moiety with a $\text{pK}_a \leq 7.4$, a carboxylic acid moiety, or an atom or group of atoms containing an O or N that binds the thyroid hormone binding pocket of a $\text{TR}\alpha$ or $\text{TR}\beta$; comprising the step of replacing E with a $-\text{P}(\text{O})(\text{OH})_2$ or prodrug thereof; and synthesizing a compound of Formula X wherein X is $-\text{P}(\text{O})(\text{OH})_2$ acid or prodrug thereof.

15

231. A method of designing a thyromimetic compound with an improved therapeutic index comprising the steps of:

obtaining a molecular formula for a thyromimetic of Formula Y:



wherein:

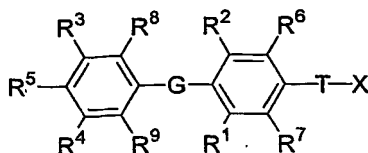
Ar^1 and Ar^2 are aryl groups;

25 G is an atom or group of atoms that links Ar^1 and Ar^2 through a single C, S, O, or N atom;

T is an atom or group of atoms linking Ar^2 to E through 1-4 atoms or is absent;

30 E is selected from the group consisting of a functional group or moiety with a $\text{pK}_a \leq 7.4$, a carboxylic acid moiety, or an atom or group of atoms containing an O or N that binds the thyroid hormone binding pocket of a $\text{TR}\alpha$ or $\text{TR}\beta$; comprising the step of replacing E with a $-\text{P}(\text{O})(\text{OH})_2$ or prodrug thereof; and synthesizing a compound of Formula X wherein X is $-\text{P}(\text{O})(\text{OH})_2$ acid or prodrug thereof.

232. A compound of Formula VIII:



wherein:

G is selected from the group consisting of -O-, -S-, -S(=O)-, -S(=O)₂-, -Se-,
 5 -CH₂-, -CF₂-, -CHF-, -C(O)-, -CH(OH)-, -CH(C₁-C₄ alkyl)-, -CH(C₁-C₄ alkoxy)-,
 -C(=CH₂)-, -NH-, and -N(C₁-C₄ alkyl)-;

T is selected from the group consisting of -(CR^a₂)_k-, -CR^b=CR^b-(CR^a₂)_n-,
 -(CR^a₂)_n-CR^b=CR^b-, -(CR^a₂)-CR^b=CR^b-(CR^a₂)-, -O(CR^b₂)(CR^a₂)_n-,
 -S(CR^b₂)(CR^a₂)_n-, -N(R^c)(CR^b₂)(CR^a₂)_n-, -N(R^b)C(O)(CR^a₂)_n-,
 10 -(CR^a₂)_nCH(NR^bR^c)-, -C(O)(CR^a₂)_m-, -(CR^a₂)_mC(O)-, -(CR^a₂)C(O)(CR^a₂)_n-,
 -(CR^a₂)_nC(O)(CR^a₂)-, and -C(O)NH(CR^b₂)(CR^a₂)_p-;

k is an integer from 0-4;

m is an integer from 0-3;

n is an integer from 0-2;

15 p is an integer from 0-1;

Each R^a is independently selected from the group consisting of hydrogen,
 optionally substituted -C₁-C₄ alkyl, halogen, -OH, optionally substituted -O-C₁-C₄
 alkyl, -OCF₃, optionally substituted -S-C₁-C₄ alkyl, -NR^bR^c, optionally
 substituted -C₂-C₄ alkenyl, and optionally substituted -C₂-C₄ alkynyl; with the proviso
 20 that when one R^a is attached to C through an O, S, or N atom, then the other R^a attached
 to the same C is a hydrogen, or attached via a carbon atom;

Each R^b is independently selected from the group consisting of hydrogen and
 optionally substituted -C₁-C₄ alkyl;

Each R^c is independently selected from the group consisting of hydrogen and
 25 optionally substituted -C₁-C₄ alkyl, optionally substituted -C(O)-C₁-C₄ alkyl,
 and -C(O)H;

R¹, R², R⁶, R⁷, R⁸, and R⁹ are each independently selected from the group
 consisting of hydrogen, halogen, optionally substituted -C₁-C₄ alkyl, optionally
 substituted -S-C₁-C₃ alkyl, optionally substituted -C₂-C₄ alkenyl, optionally

substituted -C₂-C₄ alkynyl, -CF₃, -OCF₃, optionally substituted-O-C₁-C₃ alkyl, and cyano; with the proviso that at least one of R¹ and R² is not hydrogen;

or R⁶ and T are taken together along with the carbons they are attached to form a ring of 5 to 6 atoms including 0 to 2 heteroatoms independently selected from -NRⁱ-, -O-, and -S-, with the proviso that when there are 2 heteroatoms in the ring and both heteroatoms are different than nitrogen then both heteroatoms have to be separated by at least one carbon atom; and X is attached to this ring by a direct bond to a ring carbon, or by -(CR^a₂)- or -C(O)- bonded to a ring carbon or a ring nitrogen;

Rⁱ is selected from the group consisting of hydrogen, -C(O)C₁-C₄ alkyl, -C₁-C₄ alkyl, and -C₁-C₄-aryl;

R³ and R⁴ are each independently selected from the group consisting of hydrogen, halogen, -CF₃, -OCF₃, cyano, optionally substituted -C₁-C₁₂ alkyl, optionally substituted -C₂-C₁₂ alkenyl, optionally substituted -C₂-C₁₂ alkynyl, optionally substituted -(CR^a₂)_maryl, optionally substituted -(CR^a₂)_mcycloalkyl, optionally substituted -(CR^a₂)_mheterocycloalkyl, -OR^d, -SR^d, -S(=O)R^e, -S(=O)₂R^e, -S(=O)₂NR^fR^g, -C(O)NR^fR^g, -C(O)OR^h, -C(O)R^e, -N(R^b)C(O)R^e, -N(R^b)C(O)NR^fR^g, -N(R^b)S(=O)₂R^e, -N(R^b)S(=O)₂NR^fR^g, and -NR^fR^g;

Each R^d is selected from the group consisting of optionally substituted -C₁-C₁₂ alkyl, optionally substituted -C₂-C₁₂ alkenyl, optionally substituted -C₂-C₁₂ alkynyl, optionally substituted -(CR^b₂)_naryl, optionally substituted -(CR^b₂)_ncycloalkyl, optionally substituted -(CR^b₂)_nheterocycloalkyl, and -C(O)NR^fR^g;

Each R^e is selected from the group consisting of optionally substituted -C₁-C₁₂ alkyl, optionally substituted -C₂-C₁₂ alkenyl, optionally substituted -C₂-C₁₂ alkynyl, optionally substituted -(CR^a₂)_naryl, optionally substituted -(CR^a₂)_ncycloalkyl, and optionally substituted -(CR^a₂)_nheterocycloalkyl;

R^f and R^g are each independently selected from the group consisting of hydrogen, optionally substituted -C₁-C₁₂ alkyl, optionally substituted -C₂-C₁₂ alkenyl, optionally substituted -C₂-C₁₂ alkynyl, optionally substituted -(CR^b₂)_naryl, optionally substituted -(CR^b₂)_ncycloalkyl, and optionally substituted -(CR^b₂)_nheterocycloalkyl, or R^f and R^g may together form an optionally substituted heterocyclic ring, said heterocyclic ring may contain a second heterogroup within the ring selected from the group consisting of O, NR^c, and S, wherein said optionally substituted heterocyclic ring may be substituted with 0-4 substituents selected from the group consisting of optionally

substituted -C₁-C₄ alkyl, -OR^b, oxo, cyano, -CF₃, optionally substituted phenyl, and -C(O)OR^h;

Each R^h is selected from the group consisting of optionally substituted -C₁-C₁₂ alkyl, optionally substituted -C₂-C₁₂ alkenyl, optionally substituted -C₂-C₁₂ alkynyl, optionally substituted -(CR^b)_naryl, optionally substituted -(CR^b)_ncycloalkyl, and optionally substituted -(CR^b)_nheterocycloalkyl;

R^s is selected from the group consisting of -OH, optionally substituted -OC₁-C₆ alkyl, -OC(O)R^e, -OC(O)OR^h, -F, -NHC(O)R^e, -NHS(=O)R^e, -NHS(=O)₂R^e, -NHC(=S)NH(R^h), and -NHC(O)NH(R^h);

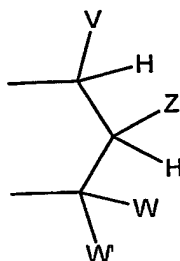
X is P(O)YR¹¹Y'R¹¹;

Y and Y' are each independently selected from the group consisting of -O-, and -NR^v-; when Y and Y' are -O-, R¹¹ attached to -O- is independently selected from the group consisting of -H, alkyl, optionally substituted aryl, optionally substituted heterocycloalkyl, optionally substituted CH₂-heterocycloalkyl wherein the cyclic moiety contains a carbonate or thiocarbonate, optionally substituted -alkylaryl, -C(R^z)₂OC(O)NR^z, -NR^z-C(O)-R^y, -C(R^z)₂-OC(O)R^y, -C(R^z)₂-O-C(O)OR^y, -C(R^z)₂OC(O)SR^y, -alkyl-S-C(O)R^y, -alkyl-S-S-alkylhydroxy, and -alkyl-S-S-S-alkylhydroxy;

when Y and Y' are -NR^v-, then R¹¹ attached to -NR^v- is independently selected from the group consisting of -H, -[C(R^z)₂]_q-COOR^y, -C(R^x)₂COOR^y, -[C(R^z)₂]_q-C(O)SR^y, and -cycloalkylene-COOR^y;

when Y is -O- and Y' is NR^v-, then R¹¹ attached to -O- is independently selected from the group consisting of -H, alkyl, optionally substituted aryl, optionally substituted heterocycloalkyl, optionally substituted CH₂-heterocycloalkyl wherein the cyclic moiety contains a carbonate or thiocarbonate, optionally substituted -alkylaryl, -C(R^z)₂OC(O)NR^z, -NR^z-C(O)-R^y, -C(R^z)₂-OC(O)R^y, -C(R^z)₂-O-C(O)OR^y, -C(R^z)₂OC(O)SR^y, -alkyl-S-C(O)R^y, -alkyl-S-S-alkylhydroxy, and -alkyl-S-S-S-alkylhydroxy; and R¹¹ attached to -NR^v- is independently selected from the group consisting of -H, -[C(R^z)₂]_q-COOR^y, -C(R^x)₂COOR^y, -[C(R^z)₂]_q-C(O)SR^y, and -cycloalkylene-COOR^y;

or when Y and Y' are independently selected from -O- and -NR^v-, then together R¹¹ and R¹¹ are -alkyl-S-S-alkyl- to form a cyclic group, or together R¹¹ and R¹¹ are the group:



wherein:

V, W, and W' are independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted aralkyl, heterocycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, optionally substituted 1-alkenyl, and optionally substituted 1-alkynyl;

or together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 atoms, wherein 0-1 atoms are heteroatoms and the remaining atoms are carbon, substituted with hydroxy, acyloxy, alkylthiocarbonyloxy, alkoxy, alkoxy, or aryloxy, attached to a carbon atom that is three atoms from both Y groups attached to the phosphorus; or

or together V and Z are connected via an additional 3-5 atoms to form a cyclic group, wherein 0-1 atoms are heteroatoms and the remaining atoms are carbon, that is fused to an aryl group at the beta and gamma position to the Y attached to the phosphorus;

or together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxy, alkylthiocarbonyloxy, and aryloxy, attached to one of said carbon atoms that is three atoms from a Y attached to the phosphorus;

or together Z and W are connected via an additional 3-5 atoms to form a cyclic group, wherein 0-1 atoms are heteroatoms and the remaining atoms are carbon, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

or together W and W' are connected via an additional 2-5 atoms to form a cyclic group, wherein 0-2 atoms are heteroatoms and the remaining atoms are carbon, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

Z is selected from the group consisting of $-\text{CHR}^z\text{OH}$, $-\text{CHR}^z\text{OC(O)R}^y$, $-\text{CHR}^z\text{OC(S)R}^y$, $-\text{CHR}^z\text{OC(S)OR}^y$, $-\text{CHR}^z\text{OC(O)SR}^y$, $-\text{CHR}^z\text{OCO}_2\text{R}^y$, $-\text{OR}^z$,

-SR^z, -CHR^zN₃, -CH₂aryl, -CH(aryl)OH, -CH(CH=CR^z)OH, -CH(C≡CR^z)OH, -R^z, -NR^z, -OCOR^y, -OCO₂R^y, -SCOR^y, -SCO₂R^y, -NHCOR^z, -NHCO₂R^y, -CH₂NHaryl, -(CH₂)_q-OR^z, and -(CH₂)_q-SR^z;

q is an integer 2 or 3;

5 Each R^z is selected from the group consisting of R^y and -H;

Each R^y is selected from the group consisting of alkyl, aryl, heterocycloalkyl, and aralkyl;

Each R^x is independently selected from the group consisting of -H, and alkyl, or together R^x and R^x form a cyclic alkyl group;

10 Each R^v is selected from the group consisting of -H, lower alkyl, acyloxyalkyl, alkoxy-carbonyloxyalkyl, and lower acyl;

with the provisos that:

a) when G is -O-, T is -CH₂-, R¹ and R² are each bromo, R³ is *iso*-propyl, R⁴ is hydrogen, and R⁵ is -OH, then X is not P(O)(OH)₂ or P(O)(OCH₂CH₃)₂;

15 b) V, Z, W, W' are not all -H; and

c) when Z is -R^z, then at least one of V, W, and W' is not -H, alkyl, aralkyl, or heterocycloalkyl;

d) when G is -O-, T is -(CH₂)₀₋₄-, R¹ and R² are independently halogen, alkyl of 1 to 3 carbons, and cycloalkyl of 3 to 5 carbons, R³ is alkyl of 1 to 4 carbons or cycloalkyl of 3 to 7 carbons, R⁴ is hydrogen, and R⁵ is -OH, then X is not -P(O)(OH)₂ or -P(O)(O lower alkyl)₂; and

e) when G is -O-, R⁵ is -NHC(O)R^e, -NHS(=O)₁₋₂R^e, -NHC(S)NH(R^h), or -NHC(O)NH(R^h), T is -(CH₂)_m-, -CH=CH-, -O(CH₂)₁₋₂-, or -NH(CH₂)₁₋₂-, then X is not -P(O)(OH)₂ or -P(O)(OH)NH₂;

25 and pharmaceutically acceptable salts and prodrugs thereof and pharmaceutically acceptable salts of said prodrugs.

233. A method of increasing the liver specificity of a T3 mimetic having a carboxylic acid moiety comprising the preparation of a compound that is an analog of said T3 mimetic wherein said carboxylic acid moiety is replaced by P(O)(OH)₂ and prodrugs thereof.

234. A method of selecting a T3 mimetic having enhanced liver specificity comprising the steps of:

- a) measuring the liver specificity of a T3 mimetic having a carboxylic acid moiety;
- b) measuring the liver specificity of a compound that is an analog of said T3 mimetic having a carboxylic acid moiety wherein the carboxylic acid moiety is replaced by a $P(O)(OH)_2$ or prodrug thereof;
- c) comparing the liver specificities of steps a) and b).
235. A method of screening T3 mimetics comprising the steps of:
- a) measuring a biological effect of T3 mimetic having a carboxylic acid moiety wherein said biological effect is selected from the group consisting of the K_i relative to T3, effects on blood glucose level, effects on serum cholesterol level, effects on fat in the liver, liver specificity, and therapeutic index;
- b) measuring the same biological effect measured in a) of a T3 mimetic having a phosphonic acid or prodrug moiety thereof; and
- c) comparing the results in steps a) and b);
- d) selecting the T3 mimetic of step b) for further scientific evaluation.
236. A compound as in any of claims 1, 2, 117, 139, 140, or 232, wherein said compound is in the form of a co-crystal.
237. The method of claim 135 wherein said metabolic disease is NASH.
238. The method of claim 135 wherein said metabolic disease is selected from the group consisting of impaired glucose tolerance, diabetes, and metabolic syndrome X.